FEBRUARY, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

The "Sodium Nicotinate Test", Its Clinical and Experimental Applications
Corticodiencephalic Gastrointestinal Syndromes in Epileptics (Part II)
Contribution to the Study of Gastric Tuberculosis
Preventive Medicine

Fifteenth Annual Convention
New York, N. Y., 9, 10, 11 October 1950

VOLUME 17 NUMBER 2

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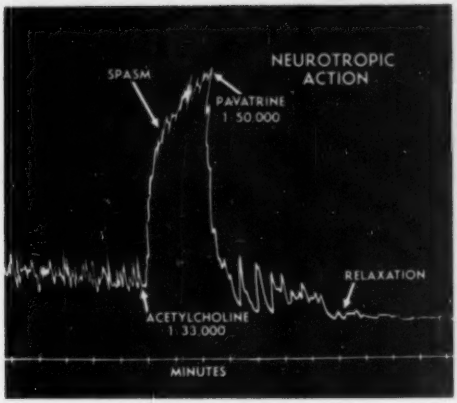

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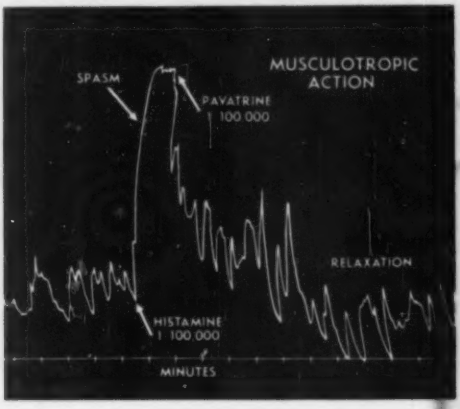

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 17 FEBRUARY, 1950 NUMBER 2

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1. Weiss, S., Espinal, R. B. & Weiss, J.: Therapeutic Application of Anion Exchange Resins in the Treatment of Peptic Ulcer, Review of Gastroenterology, 16:501-509, June, 1949.

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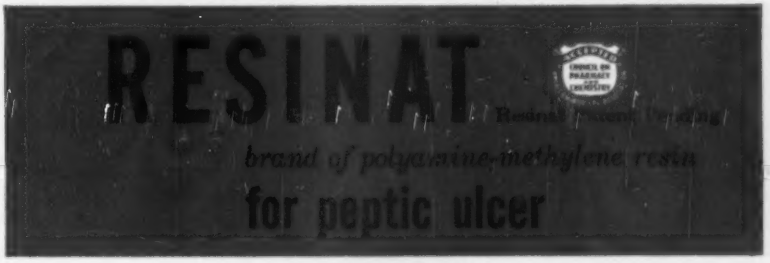

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Illustrations and diagrams should carry suitable lettering and explanations. Four illustrations per article are allowed without cost to the author.

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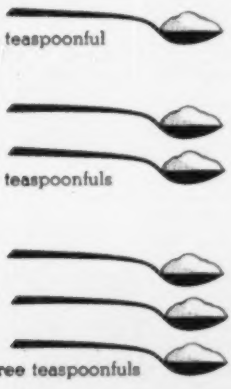

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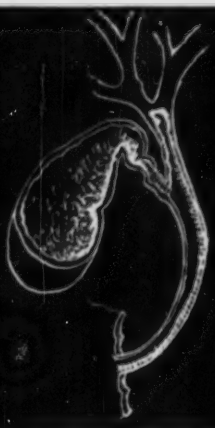

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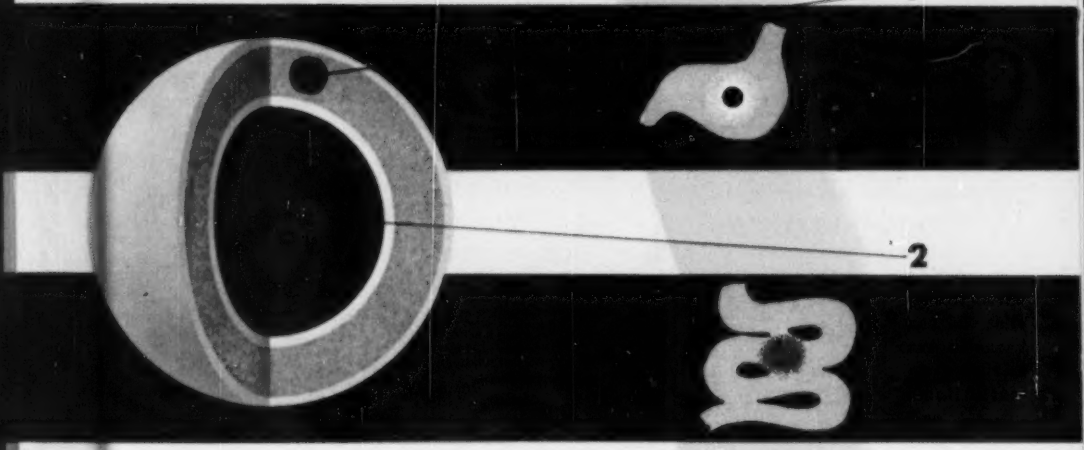

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1. McGavack, T.H., and Klotz, S.D.: Bull. Flower Fifth Ave. Hosp., 9:61, 1946. 2. Weissberg, J., et al.: Am. J. Digest Dis., 15:332, 1948.

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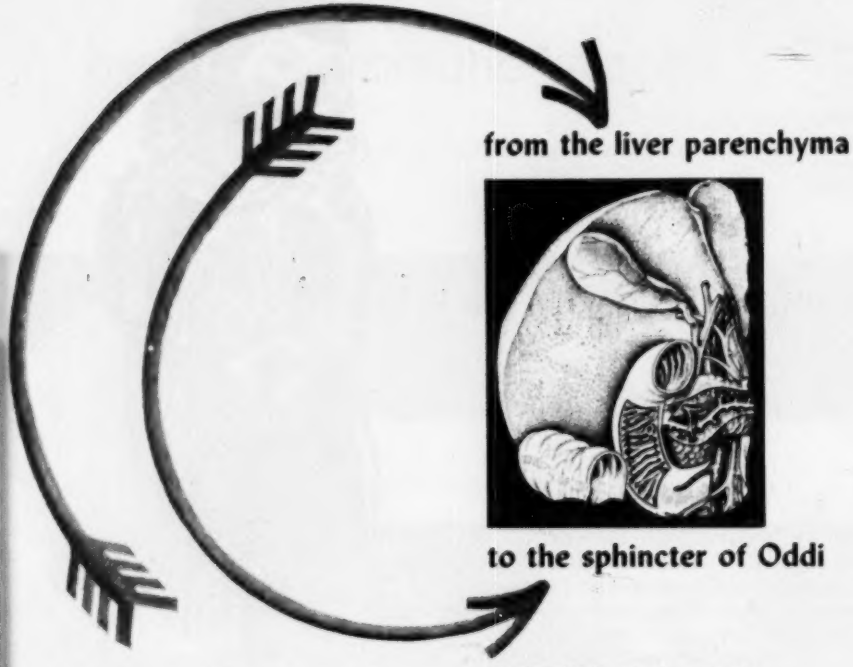

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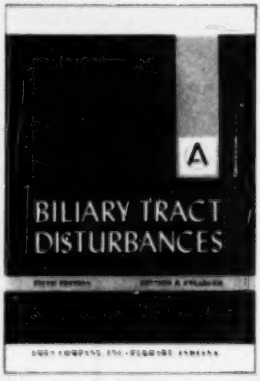

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Volume 17 FEBRUARY, 1950 Number 2

THE "SODIUM NICOTINATE TEST", ITS CLINICAL AND EXPERIMENTAL APPLICATIONS*†

A Review

Mario Stefanini, M.D., M.Sc.**
Boston, Mass.

In 1941, Villa[1], after prolonged observation of a large group of patients with different degrees of liver dysfunction, suggested that nicotinamide given orally or parenterally improved the clinical condition and the function of the liver in these cases. In particular, he observed a striking remission of jaundice in some patients, in which the liver damage had not yet reached the irreversible stage. Villa's results were later confirmed by other workers[2,3,4].

While investigating the mechanism of the therapeutic effect of nicotinamide in liver dysfunction, Mattei[5] observed that the intravenous injection of sodium nicotinate in normal subjects was followed by a transitory elevation of the level of serum indirect reacting bilirubin. He found that, following the injection of 30 mg. of sodium nicotinate, the serum indirect reacting bilirubin level rose rapidly, reaching a maximum value from 60 to 90 minutes, remained high for 2 to 3 hours and then slowly returned to normal after 6 to 8 hours. Mattei attributed the hyperbilirubinemic effect of sodium nicotinate to exaggerated hemolysis, described different curves that he considered pathognomonic of various types of liver dysfunction and concluded that the phenomenon could be utilized as a test of liver function.

This preliminary observation has been confirmed and considerably extended by the author and his associates[6,7,8]. The present review will briefly summarize the findings obtained so far with the "sodium nicotinate test" and will attempt an evaluation of their significance and applicability in the study of the physiopathology of the metabolism of biliary pigments and of the bile excreting function of the liver. The data utilized in this review have been obtained from investigations with the "sodium nicotinate test" in 25 healthy subjects and 82 patients with various disorders of the liver.

---

*Tables, illustrations and a great part of the experimental material reviewed in the present article have been previously published in the "Journal of Laboratory and Clinical Medicine" and are used in this review through the courtesy of the Editor of the journal.

†From the Department of Internal Medicine, University of Rome, Italy (Director: Prof. C. Frugoni) and the Department of Biochemistry, Marquette University School of Medicine, Milwaukee (Director: A. J. Quick, Ph.D., M.D.)

**Blood Research Laboratories, Joseph Pratt Diagnostic Hospital, Boston, Mass.

Technic

Thirty mg. of sodium nicotinate dissolved in 10 ml. of saline solution are injected slowly in a vein of the patient, who has been fasting for the past 12 hours. The injection is followed almost immediately by a sensation of warmth and flush-

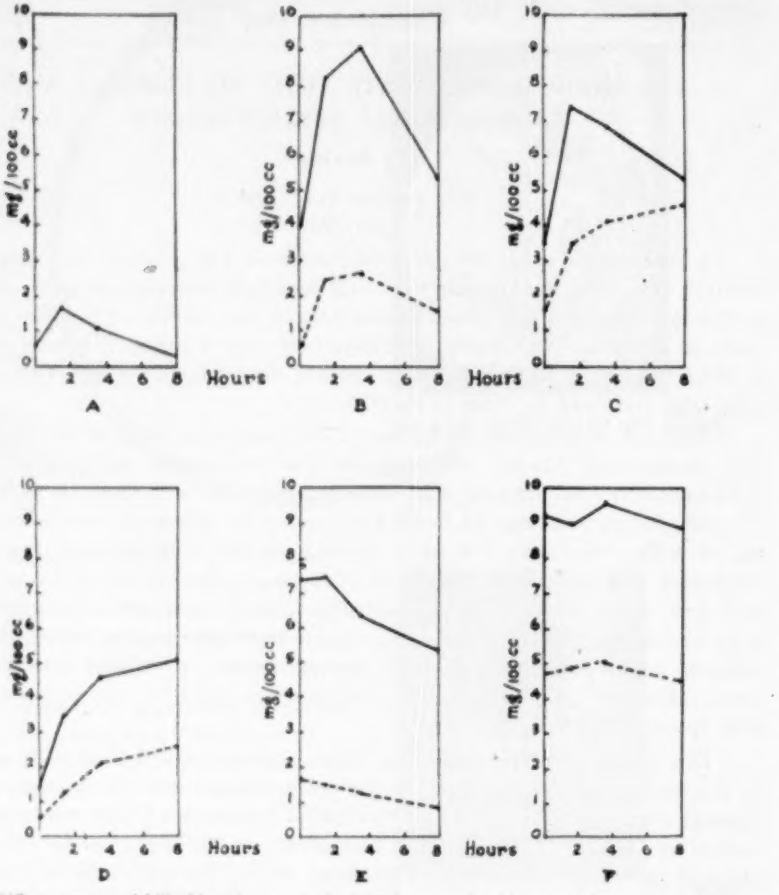

Fig. 1—Different types of bilirubinemic curves obtained in normal subjects and in patients of various liver disorders, after the intravenous injection of 30 mg. of sodium nicotinate.
(The continuous lines represent the level of total serum bilirubin, the broken ones the level of serum direct reacting bilirubin.)

ing especially in the face and limbs. Some patients also complain of mild cramp-like epigastric pains. All these effects, which are accompanied by a marked vasodilatation especially evident over the face and limbs, subside gradually in 5 to 10 minutes. Samples of blood are collected immediately before and 90, 210 and 480 minutes following the injection of sodium nicotinate. To avoid hemolysis,

a needle is first cleanly inserted in a vein of the anticubital fossa. One ml. of blood is collected in the syringe, which is then substituted by another one coated with Silicone (Dri Film 9987, General Electric Company) and 10 ml. of blood are drawn slowly, carefully avoiding foaming*. The blood is then transferred to pyrex glass centrifuge tubes, pouring it carefully along the wall and avoiding foaming. The tubes are kept in an incubator at 37° C. for one hour. At the end of this period the serum is separated by centrifugation at 2,000 r.p.m. for 10 minutes and transferred to pyrex glass test tubes which are corked and kept in the ice box at 4° C. With this technic, hemolysis, which represents the most common cause of error, can be avoided completely.

TABLE I

Effect on the Serum Bilirubin Level of the Parenteral Administration to Normal Subjects of Substances Chemically or Pharmacologically Related to Sodium Nicotinate.

Substance	Dose and route of administration	Serum Bilirubin Level (mg. %)				
		Time after injection				
		0′	30′	90′	180′	210′
Normal Control		0.36		0.32		0.43
Sodium Nicotinate	mg.30, intravenously	0.34	0.58	1.07		0.74
Histamine, hydrochloride	mg. 1, intramuscularly	0.50	0.61	.055	0.58	
Epinephrine, hydrochloride	mg. 1, intramuscularly	0.70	0.86	0.67	0.59	
Acetylcholine, hydrochloride	mg. 100, intramuscularly	0.48	0.53	0.51		0.50
Niketamide	mg. 850, intravenously	0.40	0.42	0.49		0.38
Nicotamide	mg. 100, intravenously	0.56		0.61		0.60

Not later than 8 hours after their collection, total and direct reacting bilirubin are determined in each sample of serum by the method of Jendrassik and Grof[9]. The level of indirect reacting bilirubin is represented by the difference between the other two values experimentally measured.

To avoid excessive discomfort to the patient a light meal can be served immediately after the third sample of blood has been collected, which will not interfere with the results of the test.

Results and Mechanism of the "Sodium Nicotinate Test"

(a) *Modifications of the serum bilirubin level following the intravenous injection of sodium nicotinate*:—In normal subjects the intravenous injection of

*The solution of sodium nicotinate can be injected by connecting the syringe in which it is contained to the needle inserted in the vein to collect the first sample of blood.

sodium nicotinate is followed by a rise of serum indirect reacting bilirubin level from 100 to 200 per cent. The maximum effect is reached from 60 to 90 minutes after the injection and from then on the bilirubin level slowly and gradually decreases reaching the initial value after 6 to 8 hours. If the changes of bilirubin level are followed at regular intervals of time and plotted against time, the curve obtained presents a sharp, short ascending and a prolonged slowly descending segment. Figure 1A shows an average normal curve derived from the analytical values obtained in 25 normal subjects. Variations of the level of serum cholesterol and bile salts after the injection of sodium nicotinate can also be observed in healthy subjects and patients with liver dysfunction (Table III). These variations, however, appear to be so inconsistent that no clear significance can be attached to them.

In healthy subjects, no direct reacting bilirubin appears in circulation following the injection of sodium nicotinate.

(b) *The cholagogic and choleretic action of sodium nicotinate*:—Villa's[1] clinical observations suggest that the oral and parenteral administration of nicotinic acid might determine a sudden increase in biliary flow. To substantiate this conclusion the following experiment was performed in 18 healthy subjects, all medical students. A Rehfuss tube was passed into the duodenum under fluoroscopic control and its extremity connected with a drainage bottle. Few ml. of yellowish fluid were collected at first and the scanty flow subsequently stopped altogether. Thirty minutes later, 30 mg. of sodium nicotinate were slowly injected intravenously. Ten minutes later a copious flow of bile appeared. At first, for 5 minutes or so, light colored fluid with the characteristics of bile A was collected in an amount of from 10 to 15 ml. For the following 20 minutes the bile appeared of dark brown color (bile B) and was obtained in amounts of from 175 to 200 ml. Finally, for another half an hour, a golden yellow colored bile (bile C) was collected (40-50 ml.) and at the end of the hour the flow stopped altogether. All through its excretion, the bile was ejected in rhythmical waves at the average speed of 2 to 4 ml. per minute. At the same time, serum bilirubin level failed to show the ordinary rise.

The total amount of bile collected during the hour averaged 200 to 250 ml. This amount is far greater than that obtainable when biliary excretion is stimulated with the Meltzer-Lyon technic, indicating that the stimulation on the bile excreting function of the liver exercised by sodium nicotinate is by far the most powerful available. No increase in bilirubin concentration of bile was observed in the healthy subjects studied, which would exclude a direct choleretic effect of sodium nicotinate. It might be said at this point that Decholin also used in the same experimental conditions did not seem to possess any clearly evident choleretic effect. A possibility exists, however, that sodium nicotinate might exert a choleretic effect in patients with biliary retention due to moderate liver dysfunction. In this respect it may be interesting to refer briefly to a case which has been the subject

of a previous communication[10]. The patient was suffering from chronic hepatocholangitis and biliary retention for which a surgical biliary fistula had been established. The case offered an obvious opportunity of following the modifications of the bilirubin level in serum and bile following the intravenous injection of sodium nicotinate. This procedure in the patient was followed by a limited rise of the serum bilirubin level (Table IVb). When this began to decrease towards the initial value, an evident increase of bilirubin in the bile was observed.

(c) *Changes in elimination of urobilin following the intravenous injection of sodium nicotinate*:—As the injection of sodium nicotinate is followed by increased bile excretion within the intestine and more urobilinogen becomes, therefore, available for reabsorption from the intestinal tract, a corresponding rise of urobilin eliminated with the urine should be expected. This has been shown to be the case (Table IV).

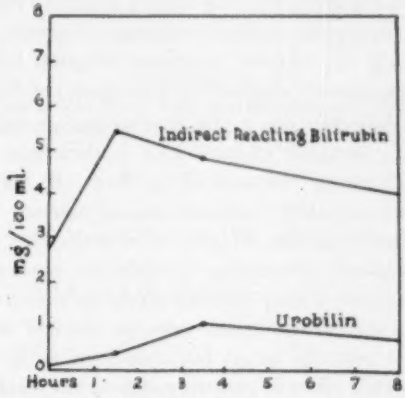

Fig. 2—The effect of the intravenous injection of 30 mg. of sodium nicotinate on the level of serum indirect reacting bilirubin and the level of urobilinuria in a patient of chronic hepatocholangitis.
(The values of indirect reacting bilirubin and of urobilin are expressed in mg. per 100 ml. of serum and urine, respectively.)

Urobilin level in urine was determined in 15 healthy subjects and 7 patients with liver dysfunction, before and after the intravenous injection of sodium nicotinate. Serum bilirubin levels were followed at the same time. Urobilin in urine was determined with a modification of the method of Heilmeyer and Krebs[11]. The urinary concentration of urobilin rose from five to eight times the original values, reached a maximum value two to three hours after the injection and then slowly returned to the initial level in about 24 hours (Figure 2). The percentage rise of urobilin concentration appeared to be roughly proportional to that of the indirect reacting bilirubin of serum, although delayed in time. In patients with dysfunction of the liver, the rise of urobilin concentration in urine following the intravenous injection of sodium nicotinate was very pronounced (from ten to fifteen times the original values) and persisted for a period of 48 to 72 hours. A good correlation

could be observed between changes in urobilin elimination and severity of liver dysfunction.

In patients with liver dysfunction in which the injection of sodium nicotinate was followed by appearance in circulation of bilirubin of the direct reacting type, a contemporary appearance or rise of the already present bilirubin was observed in the urine.

(d) *Hyperbilirubinemic curves in normal and pathological conditions*:—With the intravenous injection of sodium nicotinate determining a sudden and evident circulatory load of indirect reacting bilirubin, the problem arises of the mechanism by which the body accomplishes and regulates its elimination. It has been mentioned previously that, with the contemporary study of the level of bilirubin of serum and bilirubin of bile in a patient with surgical biliary fistula, it has been possible to demonstrate that the decrease in serum bilirubin is accompanied by increased elimination of bilirubin with the bile. It appears therefore that, in disposing of the excess of circulating indirect reacting bilirubin, the liver utilizes its capacity of transforming the indirect to direct reacting bilirubin (bile-forming function), which it consequently eliminates (bile-excreting function).

The normal hyperbilirubinemic curve due to sodium nicotinate as described in one of the preceding sections (Figure 1A) is therefore obtained when both bile-forming and bile-excreting functions of the liver are normal. A curve of this type is usually observed in healthy subjects and in patients without jaundice but moderately impaired liver function. Finally, a normal curve can also be obtained in mildly jaundiced patients presenting a moderate amount of direct reacting bilirubin in circulation (this is only insignificantly modified during the course of the test and always returns to the initial value at the end of the 8-hour period). Often at the end of the test, the serum bilirubin level is, in these patients, lower than the initial value. This effect is probably due to the cholagogic (and possibly choleretic) effect of sodium nicotinate, which stimulates a torpid but not severely compromised liver parenchyma.

In pathological conditions, all characterized clinically by jaundice of different intensity, two principal modifications may be found in the hyperbilirubinemic curve: (a) appearance in circulation of bilirubin of the direct reacting type; (b) failure of the bilirubin level to return to normal values within the experimental period of 8 hours. Different combinations of these changes appear in the variety of pathological curves which can be found. Two main types are usually encountered. In the first (Figure 1B) concentration of both total and direct reacting bilirubin rises sharply after the injection and then decreases slowly without returning to the initial values at the end of the eight hours. In the second type (Figure 1D) concentration of both total and direct reacting bilirubin rise continuously during the experimental period. Both curves indicate different degrees of impairment of the bile excreting function of the liver; at the same time, as the concentration of circulating direct reacting bilirubin also increases, the "bile forming" function of the liver must be, at least partially, preserved. An extreme example of

the dissociation of the two functions is found in some cases in which, after the initial increment following the injection of sodium nicotinate, the level of serum indirect reacting bilirubin decreases, while that of direct reacting bilirubin continues to rise (Figure 1C).

Other types of pathological curves are less commonly encountered. So, patients with complete obstruction of the biliary tract present a characteristically flat curve (Figure 1F), which will be discussed later. Finally, in two cases of jaundice due to arsenic poisoning a paradoxical curve was obtained (Figure 1E). Following the injection of sodium nicotinate, the values of total and direct reacting bilirubin remained unchanged for about 90 minutes and then dropped slowly. It is possible that this type of response is due to the stimulating effect of sodium nicotinate on a sluggish but not very much impaired bile excreting function of the liver.

(e) *The mechanism of the hyperbilirubinemia due to sodium nicotinate*:—The hyperbilirubinemic effect described in this paper appears to be specific for sodium nicotinate. The intravenous injection of other substances chemically related to

TABLE II

Total Serum Bilirubin Level, Red Blood Cell and Retaculocyte Count in a Normal Subject Following the Intravenous Injection of 30 mg. of Sodium Nicotinate.

Time after injection	0′	90′	210′	480′	24 hrs.	48 hrs.	72 hrs.
Total serum bilirubin (mg. per 100 ml.)	0.75	1.40	1.05	0.89	—	—	—
Red blood cells (millions)	4.86	5.00	4.60	4.91	4.87	4.92	4.85
Reticulocytes (per thousand)	5	5	8	5	8	13	9

sodium nicotinate (nicotinamide, niketamide) or sharing with sodium nicotinate some pharmacological effect (histamine, epinephrine, acethylcholine) causes only a moderate or no modification of the serum bilirubin level (Table I).

For purposes of interpretation, the hyperbilirubinemic curve can be divided and considered separately in its two parts. The study of the patient with surgical biliary fistula in whom the progressive decrease of the level of serum indirect reacting bilirubin was accompanied by almost synchronous rise in concentration of bilirubin in bile is direct evidence that the descending part of the curve is related to the state of the bile excreting and, possibly, of the "bile forming" function of the organ.

The pathogenetic mechanism of the ascending part of the curve is, on the other hand, of extremely difficult interpretation. The vasomotor effect of sodium nicotinate suggests that the hyperbilirubinemia might be due to mobilization of biliary pigments from tissular reserves. This hypothesis is, however, hardly tenable as, at least in normal conditions, no tissue deposits of bile pigments are known to exist[12]. Moreover, the injection of sodium nicotinate is not followed by changes in

blood levels of chlorides and uric acid, substances which are easily mobilized from tissues (Table III). Another possibility is represented by an exaggeration of normal hemolytic processes. Facts against this hypothesis have, however, been accumulated: (a) The injection of sodium nicotinate is not followed by a significant change in red blood cells or reticulocyte count over a period of 72 hours (Table II). The possibility that changes in red blood cells and reticulocyte counts might be masked by variations of hemoconcentration is apparently denied by the absence of modifications of the hematocrit reading following the injection of sodium nicotinate; (b) No increase in plasma hemoglobin concentration follows the hyperbilirubinemia at any interval of time. Moreover, patients with increased fragility of erythrocytes do not show hyperbilirubinemic curves of unusual type. It is readily admitted that these observations are not an absolute denial of the possibility that the hyperbilirubinemia might be due to exaggerated hemolysis, but the theory certainly lacks clear-cut evidence in its favor.

Another interpretation is offered by the evidence presented in the course of this paper. It appears that the hyperbilirubinemic effect of sodium nicotinate is related to the availability of the bile in the intestine. Two main findings support this conclusion, one clinical and one experimental. The clinical observation is that patients with complete biliary obstruction do not present any hyperbilirubinemic response to sodium nicotinate. Experimentally, when the bile is extracted as completely as possible from the duodenum while excreted by means of a Rehfuss tube, the injection of sodium nicotinate markedly increases the biliary flow (as previously described), but is followed by only a limited or nonhyperbilirubinemic effect. In order for this theory to stand two conditions must be fulfilled: the amount of bile excreted must be increased and the reabsorption of its components from the intestine must be more pronounced than in normal conditions. The first condition is certainly fulfilled with the demonstration of the cholagogic and, possibly, choleretic effect of sodium nicotinate. The pronounced vasodilatatory action of sodium nicotinate on the vessels of the splanchnic area probably accounts for the increased reabsorption of components of bile from the intestine. That this certainly occurs is shown by the changes of elimination of urobilin following the intravenous injection of sodium nicotinate and evidently due to an exaggerated reabsorption of urobilinogen. Evidence has also been obtained to indicate that the vasodilatatory effect of sodium nicotinate is of predominant importance in the mechanism of its hyperbilirubinemic effect. It has been said already that no significant hyperbilirubinemia follows the intravenous injection of nicotinamide. This drug, only slightly less active than sodium nicotinate in stimulating the bile flow, does not possess any vasodilatatory effect, the absence of which probably accounts for the absence of hyperbilirubinemic changes following the injection of nicotinamide.

All this evidence suggests that the increase of indirect reacting bilirubin of serum following sodium nicotinate might be due to increased reabsorption from the intestine of a biliary pigment (possibly mesobilirubin). This mechanism, if

directly proved, would have significant implications concerning the transport and metabolism of biliary pigments. It is, unfortunately, greatly at variance with the accepted theories of the metabolism of biliary pigments. The findings presented in this paper, however, agree with and support the suggestion by Zoja[13] and other Italian workers that serum bilirubin of the indirect reacting type represents reabsorbed mesobilirubin which has escaped the hepatic filter through lymph channels and porta-cava anastomoses. Even after the demonstration by Coangiuli[14] that mesobilirubin and indirect reacting bilirubin behave in a similar manner with various chemical reagents, this theory has not been given enough consideration. A direct approach is being worked out to prove or disprove it, using the "sodium nicotinate test" as a working technic.

Clinical applications of the "sodium nicotinate test":—The sodium nicotinate technic, produces a rise in the level of serum indirect reacting bilirubin which is

TABLE III

LEVELS OF BILIRUBIN, CHOLESTEROL, BILE SALTS, CHLORIDES AND URIC ACID OF SERUM IN A PATIENT WITH CIRRHOSIS OF THE LIVER, FOLLOWING THE INTRAVENOUS INJECTION OF SODIUM NICOTINATE (30 MG.).

Time after injection	0′	90′	210′	480′
Total bilirubin (mg. per 100 ml.)	3.99	8.12	9.02	5.65
Direct reacting bilirubin (mg. per 100 ml.)	0.33	1.05	1.07	0.89
Cholesterol (mg.per 100 ml.) (*)	85	130	78	71
Bile salts (mg.per 100 ml.) (**)	0	20	8	0
Chlorides (gm.per 100 ml.)	7.37	6.90	7.02	7.11
Uric acid (mg.per 100 ml.)	4.88	4.35	4.16	4.21
(*) determined by Autenrieth's method (**) determined by Cottet's method				

more conspicuous and prompt than that obtainable with several other procedures (for a critical evaluation of these procedures, reference is made to Bramante's review [15]). As mentioned previously, the test probes the ability of the liver to dispose of a large and sudden load of bilirubin, so evaluating the bile-excreting and possibly the bile forming function of the hepatocyte. Logically enough, Mattei[5] recommended the technic as a test of liver function. Unfortunately, our studies in patients with various liver disorders clearly show that the pattern of the hyperbilirubinemic curve presents no clear-cut relationship with the anatomical, clinical diagnosis of the case the total hepatic function as evaluated with a "battery" of liver function tests, or the result of any other individual test. This conclusion does not voice condemnation of the "sodium nicotinate test" and only confirms the long known fact that bilirubin excretion is widely dissociated from other hepatic functions: it may be found normal in cases with extreme liver damage and, on the other hand, involved early in rather benign conditions. The "sodium nicotinate

test" gives a diagnostically typical curve (Figure 1F) only in cases of complete biliary obstruction. In any other case the procedure should not be used as an indication of the total function of the liver or considered as a means of differential diagnosis between obstructive and hepatocellular jaundice.

A finding of clinical and experimental interest is the observation that increased elimination of urobilin will follow the intravenous injection of sodium nicotinate. From a clinical viewpoint it proves that *large amounts of bilirubin may appear in the urine through a completely physiological mechanism, in healthy subjects without any evidence of liver damage or hemolytic processes.*

Several years ago, Melli[16] showed that in dogs, any rise of pressure within the portal system, such as can be experimentally determined by direct compression or occlusion of the portal vein or pnx. of the right side, caused increased elimina-

TABLE IV

MODIFICATIONS OF THE LEVEL OF TOTAL AND DIRECT REACTING BILIRUBIN OF SERUM AND OF UROBILIN FOLLOWING THE INTRAVENOUS INJECTION OF 30 MG. OF SODIUM NICOTINATE.

Time after injection	0′	90′	210′	480′	24 hrs.
a) *Subject M.S., ♂, age 29, normal*					
Total bilirubin (mg.per 100 ml.)	0.22	0.97	0.68	0.19	——
Direct reacting bilirubin (mg.per 100 ml.)	0	0.18	0	0	——
Urobilin (mg.per 100 ml.)	0.042	——	0.526	0.372	0.058
b) *Patient N.H., age 48, ♂, suffering from chronic hepatocholangitis*					
Total bilirubin (mg.per 100 ml.)	3.46	6.02	5.48	4.89	——
Direct reacting bilirubin (mg.per 100 ml.)	1.17	1.83	1.97	1.64	——
Urobilin (mg.per 100 ml.)	0.094	0.465	1.037	0.702	0.172

tion of urobilin. It appears that, every time hypertension or vasodilatation in the splanchnic district (as in our case) allows urobilinogen to reach the general circulation avoiding the hepatic filter, an excess of urobilin will appear in the urine. These mechanisms can probably be advocated to explain the marked urobilinuria of clinical conditions (pnx. of the right side, pylethrombosis, early cirrhosis of the liver) in which liver dysfunction is absent or too limited to account for the finding and the daily fluctuations and postprandial increase of physiological urobilinuria.

Evidence has been given in the course of the paper that sodium nicotinate given intravenously exercises a powerful cholagogic and, possibly, choleretic effect. By means of duodenal intubation in normal subjects it has been possible to show that intravenous nicotinamide or orally administered sodium nicotinate and nicotinamide have a similar but less pronounced effect. The possible therapeutic use of these substances in cases with jaundice which has not yet reached the irreversible

stage is being investigated. Noteworthy success has been obtained in cases of infectious hepatitis in an early stage in which the oral administration of nicotinic acid has been often followed by critical remission of the jaundice and prompt inprovement of liver function[19]. Obviously, much more experimental evidence is required before definite conclusions can be reached.

Conclusions

1. The intravenous injection of 30 mg. of sodium nicotinate in healthy subjects is followed by: (a) a rise of the serum level of indirect reacting bilirubin, which reaches a maximum after about ninety minutes, then slowly returns to the initial value within six to eight hours; (b) almost immediate stimulation of the secretion and excretion of bile; (c) increased elimination of urobilin, which reaches a maximum two to three hours after the injection of sodium nicotinate and returns to normal values in about 24 hours.

2. In pathologic conditions, two main modifications of the hyperbilirubinemic effect of sodium nicotinate can be observed: (a) a failure of the bilirubin level to return to normal values within the experimental period of eight hours; (b) the appearance in circulation of bilirubin of the direct reacting type. Their various combinations characterize different types of curves obtained in patients with liver disorders. These curves do not appear consistently related to the anatomical or clinical conditions of the patient, and a pathognomonic flat curve is obtained only in cases of complete biliary obstruction. Therefore, the hyperbilirubinemic effect of sodium nicotinate cannot be utilized as a test of liver function or for the differentiation between hepatogenous and obstructive jaundice.

3. When modifications of the indirect reacting bilirubin level of serum following the intravenous injection of sodium nicotinate are plotted against time, a curve is obtained with a sharp ascending and a slow descending segment. The descending part of the curve is in direct relationship with the ability of the liver to convert indirect reacting bilirubin to direct reacting bilirubin and excrete it. The ascending segment is of difficult interpretation, but experimental evidence suggests that the rise in indirect reacting bilirubin of serum might be due to increased reabsorption of mesobilirubin from the intestine. This interpretation, if correct, would radically change our present concept of the metabolism of biliary pigments identifying indirect reacting bilirubin of serum with mesobilirubin reabsorbed from the intestine and escaped to the hepatic filter through lymph channels and portacaval anastomoses.

4. The increased elimination of urobilin is very likely due to the increased reabsorption of urobilinogen, because of the vasodilatatory, cholagogic and choleretic effects of sodium nicotinate. The findings prove that large quantities of the chromogen may appear in the urine even when no liver damage or hyperhemolysis can be demonstrated.

5. Both sodium nicotinate and nicotinamide, when given intravenously or orally, exert a powerful choleretic and cholagogic effect. Good clinical results, with

prompt regression of jaundice and improvement of liver function, have been obtained in early stages of infectious hepatitis by giving oral doses of nicotinic acid within the therapeutic range.

6. No hyperbilirubinemia can be determined in dogs or rabbits by means of the intravenous injection of sodium nicotinate.

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PREVENTIVE MEDICINE*

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I do not intend to present the vast amount of disease prevention accomplished by the medical profession; viz., hygiene and sanitation, water purification, excreta disposal, pure food, and recently the control of infectious diseases by the sulfa drugs, penicillin, etc.[1]

The gastroenterologist is essentially a fundamentalist, seeking the underlying cause instead of merely treating symptoms. He must have the equipment for the diagnoses of not only gastrointestinal diseases, but the circulatory system, nervous system, kidney, liver and pancreatic disorders.

In 1912, Wm. J. Mayo called attention to the possibility that hot drinks and foods might be the exciting agent in causing carcinoma of the esophagus and stomach. In 1917 he published his great paper stating that primitive man, before the discovery of fire, never developed esophageal or gastric cancer. He points out that chronic irritation is the cause of cancer; e.g., Chinese men are served when the rice is hot and frequently develop cancer of the esophagus or stomach, while the women eat later when the rice is cool and rarely have cancer in this region; locomotive engineers develop cancer of the shin; Australians, cancer of face due to exposure to hot sun rays, etc.[2].

Chief Surgeon Evarts A. Graham of Washington University, St. Louis, in a recent lecture, reported 200 cases of lung cancer, 95.5 per cent of whom had inhaled at least one package of cigarettes a day for at least 20 years.

I find that nearly all my cases of duodenal ulcer suffer from nicotine poisoning.

Pathologists have long known that cancer occurs more frequently in arteriosclerotics. A small artery is blocked and the region supplied by it no longer receives its usual nutritional elements, and the cells behave atypically, continuing to divide and multiply incessantly. Younger persons who develop cancer have either inherited or acquired syphilis producing endarteritis syphilitica. Recently they have diagnosed cancer from smears obtained from the vaginal mucosa and other surface smears demonstrating the atypical cells; otherwise, no real advance has been made.

The specialist in gastrointestinal diseases should have feces analysis for every patient regardless of symptoms; a positive occult blood reaction** may mean the

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**_Occult Blood-The Guaiac Test._ Rub up a portion of the feces in a mortar, adding water until a fairly thin consistency is obtained. Take 10 cc. of this liquid in a test tube and add 1/3 the volume of glacial acetic acid. Mix thoroughly, but do not emulsify. Now add to the extract 10 to 12 drops of an alcoholic solution of guaiac. This solution is made by dissolving one gram of the guaiac resin in 60 cc. of 95 per cent alcohol. Now add to 10 drops of hydrogen peroxide and shake. An indigo blue color indicates a positive reaction. Depending upon the degree of color, we designate one, two, three, or four plus blood reaction.

presence of cancer. However, the blood may come from gingivitis to hemorrhoids. Sigmoidoscopy should be performed on every patient, as early adenomatous polyps and cancer are safely and quickly destroyed by diathermy sparking or fulguration[3]. In hemorrhoids a specimen of feces secured by a cotton swab at the six or eight-inch level may be negative for occult blood.

The x-ray examination, occult blood reaction, and sigmoidoscopy may all be negative yet cancer of the stomach, small intestine or colon may be present. We have quite a list of patients in whom careful palpation *of the abdomen* established the diagnosis, the growth having proceeded externally without causing any ulceration of the mucosa. One notable case, a woman aged 35, came for a check-up, symptomless, all tests negative except that I had twice palpated a small mass in the sigmoid flexure and advised surgery. She went to the Mayo Clinic where all tests were negative, including palpation. However, Dr. Judd decided to operate and removed an adenocarcinoma the size of a hickory nut that had grown externally.

Since publication of my article in regard to milk in the Archives of Pediatrics in 1943, practically all pediatricians prescribe the evaporated milk[4]. It is estimated that more than 10,000 cases of undulant fever occur in this country each year. Raw milk, therefore, is unfit for human consumption. Pasteurized milk contains many pathogenic bacteria and cannot be relied upon as a safe food. Recently streptococci and the virus of poliomyelitis and other virus diseases have been found in pasteurized milk. For many years I have used the canned evaporated milk in the treatment of duodenal and gastric ulcer as well as in catarrhal and ulcerative colitis with splendid results. All of our patients with healed ulcers are instructed not to take any dairy products excepting the canned evaporated milk and they are remarkably free from recurrences.

From my article, "Clinical Research"[3]; I quote this paragraph in regard to synthetic vitamins: "So many patients presented themselves with the remark that 'I have taken these vitamins for one or two years and still suffer from malnutrition!' All that was required to restore them was a diet list of high vitamin content and giving the brewers' yeast powder, inasmuch as few persons consume enough Vitamin B food products. I presented a paper on the subject which concluded that the synthetic vitamins could not be depended upon. This opinion was later confirmed by the research work of Professor A. J. Carlson[5] as well as Professor Drummond[6] of England." They were given the question by the War Department, "Can we rely upon the synthetic vitamins for the armed forces?" The answer from both was emphatically, "No".

Brewers' yeast powder contains all of the Vitamin B-complex, furthermore, it continues its fermentative action in the small intestines and facilitates the absorption of all other vitamins and end products of food digestion. It is a splendid nerve tonic and a good adjunct in all forms of anemia. It can be given early in cases of gastric and duodenal ulcer cases, whose diets usually lack the Vitamin B, as this finely ground powder is nonirritating.

In the treatment of amebic dysentery the intravenous use of emetine, one grain daily for seven days, followed by one week of stovarsol in dosage of one tablet before each meal is recommended. This is far superior to the subcutaneous use of the emetine. Dr. Bassler has shown that in late cases resulting in fibrous inflammation of the intestinal tract surgery is indicated[7].

In the treatment of chronic constipation a simple test for colonic motility is to give the 5-grain carmine capsule, one before and one after the evening meal. The color should appear (traces at least) in the feces evacuated the following morning. The second morning the entire stool should be colored by the carmine. On the third morning there should be no trace of the coloring matter in the feces. For severe cases of atonic colon or slow motility I find the best treatment is the straight fluid extract of cascara, given in capsules because of its bitter taste. The patient regulates the dosage from twenty drops downward in a capsule before each meal. This method produces colonic stimulation and frequently the patient may get good results by small dosage. While it is true that the long administration of cascara produced black pigmentation of the mucosa of the colon, I am sure that no pathological condition results. The after-breakfast habit together with deep pressure with the hands on the left side of the abdomen is indicated in all cases of atonic colon. Spastic constipation often associated with diverticulosis can be cured by the employment of the mineral oil retention enema given at night. Purgatives are contraindicated. The oral administration of mineral oil is not advisable as its presence in the small intestine may prevent the absorption of Vitamin A and other vital food elements.

The greatest modern work in preventive medicine is the article by Timothy Leary published in 1934 on the subject of cholesterol[8]. His research proved that all the lesions of atherosclerosis are due to the presence of cholesterol. Advanced atherosclerosis is a result of years of progressive accretion. We are indebted to Bridges for a table containing the cholesterol content of practically all foodstuffs[9]; e.g., egg yolk contains 2,648 mg. per 100 g.; brains 3,700; liver 3,400; pancreas 3,120; thymus 2,300; salmon roe 2,200. Beef contains only 76; mutton 37. Egg white is the only food that contains no cholesterol. A child or young adult requires a diet of high cholesterol content, but after the age of 35, it should be reduced. I have used the method clinically since the publication of Leary's article and have secured splendid results in patients suffering from obesity, gallstones, atherosclerosis, gout, diabetes, degenerative arthritis and cataract[10]. If we could exclude from the dietary all foods of high cholesterol content in all persons after the age of 35, I firmly believe we would go back to the days of Methuselah.

Aging persons should avoid strenuous exercises, but should take deep breathing and stretching exercises. Take definite periods of rest. The Law of the Conservation of Energy applies to the physical as well as to the mechanical world. Thyroid and iodine are both cholesterol solvents.

SUMMARY

1. Every diet list should contain the words, *"No hot foods or drinks"*.

2. Caution patient against inhaling tobacco.

3. Sigmoidoscopy should be routinely performed on every patient.

4. Test for occult blood in feces should be done on every patient.

5. Careful palpation of abdomen is essential.

6. Use no milk except the canned evaporated. Avoid it in low cholesterol diets.

7. Avoid synthetic food vitamins. Prescribe brewers' yeast powder and foods high in vitamin content.

8. Feed cholesterol food to children and young adults, but use low cholesterol diet in persons over 35 years of age. Both thyroid and iodine are cholesterol solvents.

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CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

(Part II)

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Cortical Stimulation and Motor Gastrointestinal Reactions in Nonepileptics

In the preceding pages we attempted to cover the diencephalic portion of neurogenic gastrointestinal control. We will now attempt to cover the cortical portion which forms only part of the telencephalic division of the cerebrum. Even with well established pathways within the cerebral hemispheres the neurologist often finds it difficult to localize a sizable lesion. Not only in epilepsy but in the plaques of multiple sclerosis, small tuberculomas, small scars, small gummatta, etc., the neurologist who is not trained in detecting cortical lesions will be misled by evanescent findings, absence of paralysis, indefinite sensory changes, etc., particularly if the lesion does not produce a definite cerebral lobar syndrome. Therefore, if with definitely established tracts going from the cerebral cortex to the diencephalon one will find it difficult to localize a lesion it is self-evident that with mere symptoms such as one finds in gastrointestinal upsets, even though such are associated with other positive findings, it will seem a lot more difficult to localize a cerebral focal process. For the above reasons it is necessary for us to emphasize that although there is a great deal in the literature of the autonomic system and in experimental neurology and much evidence which points to the existence of pathways controlling the gastrointestinal function, there has been insufficient investigation of the literature so that the experimental neuroanatomical work might be of use to the clinician who is confronted by symptoms pointing towards gastrointestinal derangements of cerebral focal origin. In this respect it is strange to note that in their admirable work on intussusception, Watts and Fulton (1934) were indefinite in regard to anatomical structure controlling gastrointestinal activities located not only in the cortex but also in the hypothalamus.

In order to emphasize this point and its clinical importance we present the following quotation from Watts and Fulton taken from their discussion, "Pathways Involved—." "The pathways by which impulses travel from the cerebral cortex to the intestinal musculature have not been adequately studied. They are clearly ex-

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trapyramidal paths because stimulation of area number five, etc. resulted in no activity in the intestines. Polıak (1937) has shown that there are tracts from the frontal and precentral cortex to the red nucleus and substantia nigra; possibly there are tracts also to the hypothalamus." Before continuing with the above quotation, it is essential to emphasize at this point that long before the experimental work of Watts and Fulton many anatomists and experimentalists published numerous papers dealing with definite pathways controlling autonomic activity extending from the cerebral cortex to the hypothalamus. Not only autonomic but also gastrointestinal syndromes such as the uncinate, and others have been definitely described by clinicians to prove that the pathways from the cortex to the diencephalon and vice versa do exist.

With such excellent literature from which we hope to present extensive data not only on the cerebral cortex but also on the anterior nucleus of the thalamus as well as the mammillothalamic tract, mammillary bodies, the anterior and posterior commissural systems as well as the medial longitudinal fasciculus, etc., it is difficult to see why the authors mentioned above concentrate largely on the cortex in relation to the red nucleus and substantia nigra. Although the work of Spiegel and of Archambault and Fromm indicates that sympathetic as well as parasympathetic tracts control not only autonomic, but in the case of the former author even gastrointestinal functions, it is difficult to reconcile the fact that the pathways stressed by Watts and Fulton are the ones in which the anatomical literature is most deficient. One cannot leave this subject without speculating that the above experimentalists might have been influenced by the work of Spiegel, and similar papers such as those by Bechterev whom they quote, as well as by the extensive anatomical investigations of Muskens, Spiller and Mills as against all others having collaborated particularly with the last.

It is of course unlikely that Watts and Fulton were looking for centers of sympathetic and parasympathetic within the cerebral cortex regulating gastrointestinal function in the same way as Beattie and Sheehan did when the latter stated that there is strong support for the existence of a sympathetic center regulating gastrointestinal activity located in the hypothalamus. This structure as well as the others of the cerebrum is connected with the extrapyramidal pathways. Even the last mentioned two authors, though investigating hypothalamic centers, invariably stressed the fact that stimulation by strong currents might affect parts of the brain stem distant from the areas stimulated. They, therefore, believe that tracts regulating and conducting impulses governing the stomach and intestines are many although most of them converge in the hypothalamus. The idea of a limited center in relation to the convulsive attack has been exploited for over four decades. That this has been overdone is being realized by the fact that various authorities are beginning to embrace the fibre tract idea. The same applies also to the localization of gastrointestinal function in the cerebral cortex. The failure of Watts and Fulton (1934) to stress the anatomical feature of corticodiencephalic control of gastrointestinal activity is probably because they were interested largely

in the results of stimulation in the living animal rather than in the microscopic tracing of fibre tracts or in degeneration experiments. That such is the case is shown in their citing of Beattie who stimulated the lateral margin of the infundibulum, and excited markedly increased peristalsis.

These authors also referred to the work of Sheehan and Beattie who elaborated extensively on the hypothalamus. The last mentioned authority having been the first to stress the hypothalamus as a center of gastrointestinal function. In searching for pathways Watts and Fulton mentioned the works of Cushing (1932) who stimulated the hypothalamus under Avertin anesthesia, and the work of Keezer and Keezer (1927) who showed that the majority of barbituric acid derivatives act primarily upon the hypothalamic and thalamic nuclei. Such data was mentioned by the authors who stressed the facts that some experimentalists were not cautious enough in the choice of anesthetic so that the latter was instrumental in abolishing whatever gastrointestinal reactions might have been produced by cerebral stimulation. In this way they thought that valuable autonomic anatomical data that might be of clinical importance was sacrificed. Another feature of confusion which seems to direct Watts and Fulton to the extrapyramidal system almost exclusively as a source of autonomic stimulation, was the question of vagal as against sympathetic mediation. Collateral fibres from the vagus in the internal capsule may easily be conceived as connecting with the basal ganglia. The latter structures furthermore have somatotopic parts into which the vagus might fit. Watts and Fulton's ideas along these lines may be seen from the following quotation: "Although the results in our experiments of cortical stimulation after vagotomy do not admit a definite interpretation it would appear that most excitor impulses to the small intestines reach it through the vagus, but some also may reach the small intestines by way of the spinal cord and then by preganglionic fibres of the sympathetic system. Intussusception was never produced in devagotomized animals nor were we able to detect alteration of gastric secretion in such animals."

It is this anatomical indecision which seems responsible for the difficulty which the above authors met when they attempted to explain why cortical ablation produces intussusception. In order that we may understand their problems as stated above it is necessary that a verbatim citation of the definition of the term intussusception be offered in the same way as presented by the authors under consideration who referred to the definition of Fraser (1926), as follows: "the mechanical process which results in the production of intussusception is comparatively simple. It would seem that an irregularity in the conduction of the peristaltic wave is the underlying cause. A ring of contraction develops in a segment of the bowel, for some reason that is not transmitted and its persistence at one point results in the invagination of the active portion into the lumen of the passive segment lying in continuity with it . . . the contraction of the receiving bowel has one of two possible effects—it will either expel the invaginating segment in which case the danger has passed with no more symptoms than a passing colic, or, if

its contraction has been longer delayed, it will grasp the entering segment, and actually force it along its invaginating course", (Watts and Fulton). With the above definition in mind and with the analysis of Fraser's conception of the cause of this phenomenon, Watts and Fulton presented the results of their experiments on the cerebral cortex in relation to gastrointestinal motor function.

It seems that Fraser mentioned the possibility of an error in the arrangement of the splanchnic nervous system being a factor in intussusception although no study of the problem appears to have been made. Watts and Fulton, although agreeing with Fraser's definition, failed to agree with him in regard to the cause of this phenomenon particularly since there is no record in the literature of an intussusception produced by peripheral stimulation of any of the nerves to the gut. The results of the experiments by Watts and Fulton will be offered in their summary. At present it is superfluous to render detailed descriptions of the technical procedures. After presenting their data, not only on intussusception but also on various types of contraction of the cecum and the small intestines following stimulation of the premotor area of one or both cerebral hemispheres, they were at a loss to explain the neurophysiologic explanation of the mechanism of this intussusception phenomenon. Although the animals whose cerebral cortex they stimulated had previously been operated upon with the production of hypothalamic, spinal, vagal, and other lesions, they nevertheless felt that the results of their direct stimulation of the premotor areas should not produce such a complex phenomenon which is an active as well as passive combination of reactions. It was not the ordinary faradic stimulation alone which produced the vigorous intestinal contractions that puzzled them for an explanation.

Watts and Fulton found it difficult to harmonize this fact with the occurrence of intussusception following the removal of the premotor and adjoining areas of the cortex. It is evident that they could not understand why a cortical ablation should excite rather than depress motor activity in the gut. At this point it is important that the reader understand that we are not going too far afield into experimental data when we concentrate on the effects of irritation and ablation, etc. Most cortical gastrointestinal lesions in epileptics fall into one or the other category.

The importance in the solution of their problem as stated above, as well as the necessity of elaboration of material which tends to elucidate the corticodiencephalic may be seen in the following quotation from Watts and Fulton: "a possible solution to the paradox has come from a survey of the relevant literature which has indicated that the representation in the cortex includes both excitatory and inhibitory units. Cortical ablations appear to cause enhancement of motor activity through the release from the inhibitory components and through a generalized disturbance of the delicate balance normally existing between these mutually antagonistic elements". Our authors then follow with a series of analyses of the literature on the subject of intestinal contraction as a result of stimulation of the cerebral cortex. Their first consideration is the effect of faradic stimulation. Follow-

ing this they proceed to the literature on the effects of cortical ablation. This is followed by a discussion of intussusception and skeletal movements as related to gut movement. The student of epilepsy is well aware of the existence of cortical irritative gastrointestinal lesions in individuals suffering from convulsions. In such patients ablative lesions such as cysts and other defects exist. It should therefore not be surprising if aurae pointing to the location of such lesions are of a gastrointestinal character.

Although the average laboratory investigator prefers to shy away from anything that does not produce tangible results of an extensive nature, it should be emphasized here that it is the duty of the clinician to regard as important every evidence of sympathetic imbalance no matter how small. This is particularly true in observations made of the drooling of patients afflicted with mesencephalic encephalitis. This phenomenon of salivary hypersecretion may be noted not only with the mesencephalic type of lesion but is often found associated with other evidence of diencephalic involvement such as loss of hair, facial suffusion, seborrhea, etc. in individuals suffering from lethargic encephalitis. This phenomenon of salivary and dermal hypersecretion is also seen in patients suffering from cerebral palsy. It therefore, becomes the duty of the neurologist not to disregard the works of Pavlov, who measured the amount and frequency of salivary response after producing small and large cortical lesions, in order that we might know about the relationship between the cerebral cortex and salivary as well as gastric secretion. It is unfortunate that the work of Pavlov and his 300 pupils is not incorporated sufficiently in the great realm of neurophysiology but has been largely aligned with psychological publications. Whether or not gastric or salivary secretory phenomena are studied in their relation to cortical functioning, it is important to stress here that according to this great investigator almost every lobe of the cerebrum directly or indirectly takes part in the gastrointestinal functions described above. It is therefore somewhat surprising that Watts and Fulton did not refer more often to the results of Pavlov particularly in relation to cortical ablation experiments in which the Russian physiologist's work abounds. The answer to this is probably found in the fact that Watts and Fulton were more interested in the motor rather than the secretory phases of their experiments and that Pavlov and his associates did not stress enough of the former type of experiment in their works. Pavlov's experiments followed the work of Schiff (1867).

Watts and Fulton in their presentation of the literature dealing with results of cortical function in relation to gastrointestinal contractions, although they neglected the experiments of Pavlov, mentioned and repeatedly referred to the investigations of Bechterev. According to them this great anatomist, neurophysiologist and clinician was among the first to study the relationship between the cerebral cortex and the diencephalon. From his earliest writings it seems that his interests were often occupied with the basal ganglia as well as with the aforementioned structures in their relation not only to the autonomic in general, but to the

gastrointestinal tract in particular. In respect to the basal ganglia it is interesting to note that in his investigation Bechterev favored their relation to gastrointestinal function. This is seen in his segregation of the nucleus caudatus and putamen from the globus pallidus. It is also evident in his discovery of fibres connecting the globus pallidus with the corpus subthalamicus of Luys. It is furthermore of interest to note that Bechterev studied, together with Pavlov, expressive movements and the natural reflexes responsible for the secretion of gastric juice at the sight of meat. He studied the cerebral cortex in its relation to secretion of saliva, gastric juice, bile, tears, kidney excretion, and perspiration, as well as the relation of subcortical ganglia to dancing movements.

Although over three quarters of our references to the literature to be presented subsequently consists largely of the cortical and diencephalic fibre tract formations connected directly or indirectly with gastrointestinal functioning, we feel that even more than that could be assembled not only by laboratory investigators but also neuroanatomists, if more attention were to be paid to the pioneering work of both Pavlov and Bechterev. Although the former was purely a physiologist, his work on the cerebral cortex seems of greater importance than the observations of Bechterev who concentrated more on the deeper structure of the brain in relation to the autonomic. Bechterev studied and elaborated upon mimicosomatic movements in their relation to the secretion of sex hormones and to the acceptance or refusal of food by animals. He furthermore attempted to study a relationship between general tonus in its reflection upon sympathetic tonus. Here it is important to emphasize that our analysis of the literature of gastrointestinal findings in epileptics dealt largely with such phenomena as shown on x-ray. In other words, variations in tonus of the gastrointestinal tract resulted in aurae associated with dilatations or contractions of the stomach and intestines.

In their study of the effect of faradic stimulation Watts and Fulton concentrated on the work of Bochefontaine (1876), Hlasko (1877), Openchowski (1889), and finally on the writings of Bechterev and Mislawski (1889-1890). They referred to strong peristaltic contractions resulting from stimulation of the premotor area. They particularly cite Openchowski who stimulated the cruciate sulcus from which he obtained opening of the cardia and closing of the pylorus. Such results were also obtained by stimulation of the corpora quadrigemina, corpus striatum, and the lenticular nucleus. Although the title of our paper deals with corticodiencephalic fibre pathways and the experiments of Watts and Fulton deal exclusively with the cerebral cortex, from the above it is evident that other parts of the telencephalon such as the dorsal thalamus serve as way stations for the neurogenic control of gastrointestinal function. This is seen by referring to the structures mentioned in the last sentence. It is furthermore noteworthy that such modern anatomists as Tilney and Riley (1921) stress the corpora quadrigemina as specific centers of gastrointestinal regulating structures when they stressed the frontal lobe for feeling tone.

Finally, Watts and Fulton stressed the work of Bechterev and Mislawski. By faradic stimulation of the sigmoid gyrus and the area posterior, these authorities

were able to change the condition of the intestinal musculature. The value of elaboration upon the importance of cortical anatomy as studied by the Russian investigators is shown in the obtaining of gastrointestinal responses by their extension of stimulation to the posterior portions of the brain by these authors. Bechterev and Mislawski found that occasionally the occipital regions gave similar results, but stimulation of other areas was entirely without results. The usual effects were an alteration in tonus and an increase in peristaltic activity of a few loops of intestine. Stimulation excited contraction and relaxation of the small intestine followed by similar movements in the large intestines. Osipov (1898) also worked on the sigmoid gyrus anterior to the cruciate sulcus. While stimulating in the same area Von Pfungen (1887) found an increase as well as an inhibition of peristaltic movement. Here it is sufficient to close the discussion of results obtained by faradic stimulation with the statement that Watts and Fulton (1934) obtained the same results as the authorities menioned above. They found that cortical stimulation sometimes produced peristalsis in the small intestines. In some animals activities could be obtained only in the large intestines. They state that usually intestinal motility could be influenced from most of the premotor area, often from the prefrontal region and occasionally from the postcentral gyrus. Although Watts and Fulton concentrated upon ablation experiments it should be realized that the data given above is far more important than any of the subsequent material since most laboratory investigators as well as neurosurgeons such as Penfield, etc. rely more upon stimulation effects rather than those obtained by ablation experiments. Here we must again remind the reader of the frequent occurrence of irritative and ablative lesions in the cortex of epileptic patients (Fitch, T. S. P., Weingrow, S. M. and Pigott, A. W. 1938-1948).

Before proceeding with a presentation of the final data of Watts and Fulton on ablation and release of function it might be well to present a clinical point of view in regard to certain explanations of physiologic interpretations of gastrointestinal and other phenomena that one frequently observes in epileptics. In the paper of the above authors we notice a reference to Adrian (1930) dealing with nerve conduction phenomena incidental to injury of mammalian nerve fibres. Conduction phenomena are often encountered in epileptics who present cortical lesions and gastrointestinal syndromes. Associated with the gastric and abdominal aurae in epileptics one often observes the presence of conduction symptoms which have had no explanation in neurology. For example, we find funny feelings in the stomach going to the head, feeling of electricity going to the temple, feeling of numbness in the stomach travelling up, feeling of cold or hot pain travelling toward the head from the pit of the stomach, etc. In his monumental work on myoclonic reflexes in epilepsy, Muskens claimed that the convulsion, whether tonic or clonic, is very much related to the bioelectric discharge in the myoclonic reflex. Although he was a great neurophysiologist and a much greater neuroanatomist he never attempted to give a bioelectric explanation of myoclonic shocks. The phenomena of travelling sensations were however very curious to him. He therefore invariably made note of the presence in epileptics of certain sensory excursions in his neuro-

logical findings. He stressed the works of Oppenheim and the findings of Brown-Sequard as well as those of Gowers in the above respects. In the ordinary neurological examination or history-taking one seldom finds instances of travelling touch sensations or of sensory findings that are present one day and absent the next day although the main manifestations of the disease persist. Yet in epilepsy such is the case as the authorities mentioned have claimed. These phenomena which we will syndromize, furthermore occur in relation to gastrointestinal motor aurae, etc. In the interpretation of the gastrointestinal and nongastrointestinal findings in epileptics one could, therefore, connect modern conceptions of reflex and sensory findings in relation to transmission frequencies in the myelinated and nonmyelinated fibres. This could be done particularly if signs connecting with the same are related to a fit which can and does cause a change in the electroencephalogram and is therefore a pure bioelectric event. Such phenomena invariably fall into sensory and motor categories and when associated with gastrointestinal sensory aurae invariably point to localizations other than the extrapyramidal system as represented by corpus striatum syndromes.

In clinical neurology we often find it difficult to interpret simple items such as pain, vibratory, tactile, and stereognostic sensation on a bioelectric basis. This also applies likewise to reflex changes. Although attempts have been made to interpret the fit on a bioelectric basis, and Muskens in particular has spoken of the myoclonic reaction as a discharge of potential, we are as yet very far from a complete understanding of many of the fundamental facts behind the above and of motion and sensation. Whether we deal with clinical or laboratory material the gastroenterology of epilepsy or the neuroanatomical interpretation of the effects of ablative lesions, we should remember the dictum of Pike (1931), that no one has ever been able to record a nerve impulse from a dead cell. It seems therefore that stimulation along specific pathways might be more important than overconcentration on the cerebral cortex to which they lead.

Dealing with the effects of ablation experiments on the gastrointestinal tract, Watts and Fulton cite the work of Ott and Field (1879), the observations of Bechterev (1911), the reports of Lurje (1931), and finally the results of extensive experimentation consisting of destructive lesions in the cerebrum as well as the brain stem performed by Pal and Berggrün (1888). The observations made by Watts and Fulton as well as by the other authors are crucial, since they connected motions in the gastrointestinal tract with that of skeletal muscles resulting from prefrontal and precentral brain injuries. We therefore quote their work as follows: "Ott and Field, Bechterev, Lurje, Pal and Berggrün, and our own extirpation experiments show certain parts of the cerebral cortex, i.e., the sigmoid gyrus and its neighborhood in the dog and cat, and the premotor area and its neighborhood in the monkey normally exert an inhibitory influence upon intestinal motility."

Watts and Fulton's assembled data however gives in outline every phase of the neurogenic control of gastrointestinal motility. This may be seen from the following: "When the influence of the cortex is removed by extirpation, a release of function occurs allowing excessive and perhaps abnormal intestinal motility . . .

release of function raises the question of irritation. The observation of Bechterev (1911) that defecation occurred soon after the brain stem was sectioned behind the thalamus might be accounted for on the basis of irritation . . . Sherrington's work on decerebrate rigidity (1906) spinal transsection indicates, moreover, that irritation from a transsection of cord or cerebral substance rarely lasts more than ten minutes. Ruch and Watts (1933) who demonstrated the release of function in the fore limbs extensor muscles following postbrachial and spinal transsection, find that similar signs of irritation disappear within ten minutes after the lesions were made."

Watts and Fulton, who evaluated the literature on the basis of their own experience, covered the problem of the neurogenic mechanism of intussusception so completely that we will present their data in relation to those of a number of other workers. In doing so we must emphasize that our interest is not merely in an individual symptom such as intussusception but in those of the entire intestinal tract from the view point of movements in relation to the cerebral cortex. When Watts and Fulton attempt to make connection between skeletal movements in relation to intestinal movements, we feel that it is high time that other workers followed in their footsteps, particularly those research workers who are interested in epilepsy, since the convulsive and myoclonic movements occurring in a fit are related to and controlled by the same cortical centers that are responsible for the motor manifestations of everyday activity. One begins to wonder whether the extensive cerebral cortical involvement seen in a large percentage of epileptics might not be a factor in producing gastrointestinal changes. If such be the case it is not irrelevant to assume that some of the gastrointestinal findings noted on autopsy in epileptics by Pigott, Weingrow and Fitch (1939-1940) could be explained on the basis of cortical irritation of long-standing.

In summarizing the data on the cortical neurogenic production of intussusception it is therefore noteworthy to emphasize that Nothnagel (1882) reported that the intussusceptum portions of the gut lying below the point of stimulation, folds back a segment over the contracted intussusceptum lying above when he stimulated the intestine by placing a crystal of sodium chloride in the peritoneum. The work of Mall (1896) and that of Cannon (1911) is furthermore cited in illustrating the principles of the mechanism of the central neurogenic basis of intussusception. The discussion is finally summarized with the statement that peristalsis would be another example of mutual adjustment of antagonistic muscles for efficient action. Sherrington's principle of reciprocal innervation is adduced to show that the neuromusculature of the gut obeys the same principles, noted in the functioning of striped muscles. The following quotation from Watts and Fulton is presented to show that there is a close relationship between autonomic and somatic functions in the above respect. "When the premotor area and adjacent paths of the cerebral cortex are stimulated or excised, this local reciprocal innervation appears to be disturbed. In a group of animals the resulting imbalance was sufficient to excite the production of an intussusception." If reciprocal innervation principles are brought forward to relate intestinal movement with those of striped muscles it becomes a

matter of great importance to realize that a similar comparison might be made between the function of smooth muscles of the genitourinary tract as well as those of the cardiovascular system. Before elaborating on the genitourinary tract we will eventually cite verbatim the above connections in relation to the gastrointestinal tract. The motor components of a convulsion might therefore also be seen as a universal motor response involving smooth muscle as well as striped muscle contractions and other accompaniments of the first.

The relationship between visceral and somatic functions within the cerebral cortex as drawn by Watts and Fulton is not a new one. Many such references were given by Spiegel (1932). The motor area and premotor regions contain nerve cells which were shown to govern smooth muscle action of the intestines and other viscera. This area was also alleged to be connected with blood vessels, sweat glands and salivary glands. Cortical centers which innervate skeletal muscles were said by Spiegel to have a close topographic relation to visceral organs innervating the urinary bladder and containing a center for the hip joint musculature at the same level. The center in the motor area which controls the fit musculature was also said to be controlling the act of micturition. Spiegel further stated that from the frontal cerebral cortex to the globus pallidus or to the thalamus there are fibres that are part of both the pyramidal and extrapyramidal divisions of the centrifugal vegetative tract. He placed the vegetative fibres within the lateral spinothalamic tract. Spiegel further offered a number of references to the literature dealing with transsections of various portions of the nervous system to support his contentions. One cannot overemphasize the clinical importance of the relationship between vegetative phenomena and certain aspects of skeletal and smooth muscle tonus and motion. There seems to be something fundamental in the above relationship. The neurosurgeon who has confined his attention mostly to cerebral neoplastic disease does not often appreciate the relationship stated above. The rapid increase in intracranial pressure by neoplastic growths often obscures neurologic syndromes. This does not occur in the nonneoplastic lesions. The above phenomenon seems to fall into one of three categories. A cerebral lesion may be a quiescent one depending upon its size and location. It may on the other hand be productive of certain motor phenomena which may be associated with vegetative manifestations. In the last category we find the vegetative manifestation of Parkinson's lethargic encephalitis. In that instance one sees autonomic disturbances associated with generalized hypertonicity. Under the circumstances of the occurrence of abnormal movements such as may be seen in chorea, dystonia, or generalized rigidity with tremor, we may observe vegetative phenomena but rarely see convulsive phenomena. In the above instances, disturbances in motion as well as in muscle tone seem to come first. For some unknown reason convulsive phenomena do not supervene in the above dyskinetic conditions, but vegetative manifestations are known to occur. In epilepsy on the other hand, we find vegetative manifestations associated with tonoclonic abnormal involuntary movements of a paroxysmal nature which not infrequently ends with the general hypertonicity seen in the familiar picture of neurosomatic deterioration. Considering the problem of the somatic in relation

to the vegetative the following analysis offered by Watts and Fulton in regard to skeletal muscle action is therefore in order.

"Relation of skeletal movement to gut movement . . . since the induced activity of the intestines in our experiments was usually asociated with slow rhythmic movements of the extremities (from premotor stimulation) the question arises whether the increased intestinal movements have any relation to the movement of the skeletal muscles. It seems improbable that contraction of the skeletal muscles could be a primary stimulus. Faradization of area four caused vigorous movements of the contralateral extremities but was without effect on the intestine. Also, stimulation of the postcentral gyrus and the frontal region anterior to area four produced increased motor activity of the intestines but no activity of the extremities.

"In several experiments when the anesthesia became light, struggling movements occurred as ether was removed and this was associated with marked augmentation of intestinal activity similar to that seen in response to stimulation of area six. As the depth of anesthesia increased, intestinal movements decreased." With the above, Watts and Fulton allow the reader to draw his own conclusions about the possible synchrony between many types of skeletal movements and the accompanying gut movements. One's imagination immediately gets to work about similar relationships to the movements seen in chorea, dystonia, athetosis and myoclonia. Such findings militate against Rosett's analysis of the convulsive movements as consisting of patterns of volitional and spontaneous movements.

Before summarizing the results of Watts and Fulton, the reader should realize that from the standpoint of cortical control of intestinal activity there are only certain features that are important; namely intestinal responses of the sphincteric and nonsphincteric type. Such types of reaction indicate parasympathetic stimulation or depression. It is further of interest to note which parts of the cerebral cortex are involved in the elicitation of the responses mentioned above. Although the postcentral is also found to produce gastrointestinal reaction and according to early writers even the opercula is responsible for such, it seems that Watts and Fulton stressed almost exclusively the premotor and motor as well as other portions of the frontal regions. The basic principles behind the pathologic mechanism of movements, intestinal or otherwise, will not be cleared up until the neurologist understands the neurophysiologic relationship between afferent mechanical kinetics and those of bioelectric transmission and modification and phenomenon of motion as well as sensation in the autonomic system.

In an epileptic patient in whom we can locate a lesion in the areas given above as well as in other parts of the cerebral cortex controlling autonomic gastrointestinal function we can expect the disturbances in the gastrointestinal tract as given by Watts and Fulton to occur not only during, before, or after, but also between attacks of a convulsive, petit mal and psychomotor nature. Following is a summary of the experimental data as given by Watts and Fulton stressing chief facts in cortical stimulation.

"1. The relation of the cerebral cortex to the motility of the gastrointestinal tract has been studied in a series of monkeys who had lesions made in various parts of cerebral hemispheres. Intussusception with fatal obstruction occurred spontaneously in three healthy monkeys in which the region of the premotor (area six) cortex had been removed from both hemispheres.

"2. Carefully controlled faradic stimulation of the monkeys' cortex in the premotor region gives rise to active peristaltic movements in the gut, and in two experiments with continuous stimulation (one to two minutes) well marked multiple intussusceptions were produced by this procedure. In three instances stimuli were supplied intermittently over a period of several hours and multiple intussusceptions were found on opening the abdomen.

"3. Stimulation, brief and prolonged, of the motor area (area four), which gives rise to vigorous movements of the skeletal musculature, failed to influence the movements of the gut.

"4. Stimulation of the premotor area from certain points relaxed stomach sphincters.

"5. Although intussusception was never obtained after the vagi were sectioned, stimulation of the premotor area in such preparation occasionally caused slight decrease in peristaltic movements.

"6. In some experiments cortical stimulation caused increased secretions of the gastric juice.

"7. In one instance stimulation of the frontal and postcentral convolution in the monkey in which the premotor area had been removed five months before, caused increase in peristaltic movement but no intussusception.

"8. It is concluded that the cerebral cortex of monkeys contains autonomic representation for the gastrointestinal tract which is largely restricted anatomically to the premotor area, and that this representation includes both excitatory and inhibitory components."

From the above detailed and almost complete analysis of the literature by Watts and Fulton it becomes evident that when an epileptic patient complains of gastrointestinal disturbances that are of a paroxysmal character, whether associated with the fit, coming before it, or in the period between convulsive attacks, there must be some focal lesion responsible for the same. This lesion does not necessarily have to be a brain tumor but other type of pathology, brain scars, brain atrophy, small tuberculomata, small syphillomata, meningeal adhesions, the result of trauma, etc. might produce gastrointestinal motor and secretory as well as sensory aurae. The modern literature on epilepsy offers a record of extensive vascular, meningeal and cortical pathology even in the so-called idiopathic epilepsies. All the above can produce symptoms referring to the gastrointestinal tract. That such can be the case has been definitely shown by Frazier, Watts, and Uhle (1934) in the following quotation: "Evidence presented by them (Watts and Fulton 1934) stated that cortical representation of the gastrointestinal tract contains both excitatory and inhibitory components." Watts and Frazier (1935) then showed

that gastric aurae and other visceral sensations are associated with focal convulsive seizures or usually occur independently, and after the fit. Extensive elaboration of water metabolism in relation to centers of gastrointestinal activity controlled by the hypothalamus has been referred to in preceding pages. The control of this as well as the function of urination may therefore be extended into the cerebral cortex just as the gastrointestinal functions have been. Our present work does not permit more extensive clinical elaboration on this subject of water metabolism and urination in relation to cortical stimulation. Whatever literature there is may be found in the paper by Frazier, Watts and Uhle a quotation from which follows:

"In a recent analysis of (105) verified frontal lobe tumors at the University hospital Frazier (1933) found that incontinence of urine had been observed in 19 per cent of the patients. Though incontinence might have been attributed to aphasia, indifference, or mental changes in some patients, it did not appear to explain this symptom in others. Often a patient was rational, well oriented, without signs of mental deterioration, and yet never asked for a urinal and his bed clothes had to be changed several times a day. Two patients did not know that they had voided until they became aware of their wet clothing. A third, when asked why he had voided in bed, replied that he had to urinate and could not wait."

In their work on urinary control Frazier, Watts and Uhle present data on hypertonic bladder associated with periodic incontinence of two weeks duration in a case of glioma of the genu of the corpus callosum. They also present a case of hypertonic bladder associated with incontinence of six weeks duration in a patient suffering from a verified frontotemporal glioma. These investigators also presented a case of hypertonic bladder associated with incontinence of urine of one year duration in a patient suffering from symptoms of tumor in the diencephalon. The films (ventriculographic) of this patient showed a filling defect in the posterior part of the third ventricle.

Although in the presentation of our material in later pages we cannot hope to approximate various technical procedures presented by Frazier, Watts and Uhle on the tonic types of bladder disturbances, we feel nevertheless, that the aurae presented by our patients referring to the urinary function are more numerous than those which the above authors have collected. We hope to segregate into only one syndrome group all those patients who present cerebrogenic aurae pointing towards the urinary tract. Some of the cases to be analyzed will also show gastrointestinal aurae in association with urinary. In this group syndrome we will give evidence, in addition to the urinary and gastrointestinal aurae, of concomitant focal epileptic attacks associated with or without loss of consciousness. Head movements, eye movements, sensory phenomena and various other patterns of attack will be presented to give a definite localizing place to the cerebrovisceral and viscerocerebral cortical lesions. In addition to the above, wherever possible, we will offer data of an etiologic nature that might point to the pathology of the lesion. Some of our cases falling into the epigastric and abdominal pain and peculiar feelings are not so-called referred sensations, but result from vigorous,

and, perhaps, abnormal cerebrogenic urinary tract movements. Another sensation, namely, morbid hunger associated with brain tumors, cerebral vascular disease and accidental injury to the brain, was considered by Watts to be due to irritation of the gut representation in the cortex. Some of the above were also seen in cases with urinary aurae.

In discussing the pioneering work of Watts and his collaborators on the gastrointestinal tract in its relation to movements in association with many skeletal muscle, and visceral activities as controlled by the cerebral cortex, we cannot refrain from adding other relevant comments. Volumes can be written on the comparative neuroanatomy of the frontal lobe and its relation to rhythmic chewing movements, salivation, eye movements, head and craniocervical movements, tongue action, and finally vocal responses. The above are not only related to visceral control of the cortex emanating from areas four and six but also to activities of other parts of the cerebral cortex. From the literature on the anatomy of the nervous system in relation to the gastrointestinal tract to be elaborated on by us, it will be shown that the cry preceding an epileptic fit may be localized not only in the thalamus, but also in regions adjacent to those presented by Watts and his associates. This is amply proven in books on the comparative anatomy of the representation of rhythmic chewing, vocalization and facial expression as controlled by the premotor area in lower animals. Just as the paroxysmal cry of the epileptic may be shown to have a focal representation so does the occurrence of urination before and probably during epileptic attacks.

In spite of the excellent data presented above on the cortical regulation of gastrointestinal and urinary functions there is one outstanding deficiency. This is the indecision with regard to specific tracts transmitting the impulses to and from the cerebral cortex to these structures. We shall therefore proceed to neuroanatomical data for a proper orientation regarding such and other cerebral gastrointestinal regulating structures and pathways.

(*To be continued*)

CYANOSIS FOLLOWING USE OF ANESTHESIN (ETHYL-AMINO-BENZOATE)

(Case Report)

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Careful review of the literature fails to reveal the report of a single untoward reaction from the use of ethyl-amino-benzoate (Anesthesin). The author and many of his colleagues and others, too, have used the drug frequently for its local effect on the stomach particularly. The drug, prepared as a powder, is given alone, or in combination with other ingredients. It has a numbing effect on the base of the tongue when taken in 5 or 10 grain doses and has a definite anesthetic effect on the stomach, especially in pain or nausea. The United States Dispensatory says "it is remarkable among local anesthetics for its poor solubility and its lack of toxicity"[1].

In 1924 the Committee on Therapeutic Research of the Council on Pharmacy and Chemistry reported the results of its investigation on deaths caused by the use of local anesthetics. Anesthesin was not one of the drugs mentioned in this series. Little information therefore is available about the possible toxic effects of this drug although it is very widely used especially as stated, for its effect on the pharynx, esophagus and stomach.

The author believes his personal experience with three cases and another by verbal communication from a colleague warrants publication. The first case was a young man with abdominal pain incident to an ulcer and with consequent nausea. One dose of 5 grains was given at 11 A.M. and cyanosis developed at 2 P.M. Another case was a "clinic" patient who was given a powder containing but 2½ grains of this drug with a similar result. These two cases occurred within a year, about 10 years ago.

The third case developed recently. A patient with a gastralgia, also incident to an ulcer was given 5 grains in a powder—(in this case with papaverin and phenobarbital) and developed cyanosis in a few hours. Personal communication from a colleague presented another similar story. It is of interest that all four cases were males, whose ages ranged from 18 to 55, all of whom were in good physical health and who presented pains, or pain and nausea as the only symptoms.

The onset of the cyanosis was not attended by any change in well-being and any objective phenomena other than the blueness which was marked.

In the author's three cases, because of lack of appreciation as to the probable cause and the speed with which the cyanosis disappeared, no chemical or blood spectroscopic studies were made. The cyanosis cleared completely within a few hours. In the fourth (colleague's) case, all chemical tests for the usual causes for cyanosis were entirely negative.

A recent article discussing the drugs producing met- and sulfhemoglobinemia does not include anesthesin in its listing[2].

Although without definite laboratory proof, the author believes the cyanosis to have been the result of a toxic met-hemoglobinemia in susceptible individuals. He has but one supporting reference in his favor, a minor foot-note in a text-book on pharmacology. Here was noted the belief that "ethyl-amino-benzoate may under certain conditions by absorption from the intestinal tract, induce met- or sulfhemoglobinemia."

This report is being made, not to discourage the use of this agent whenever or wherever indicated but rather to draw attention in its use, to the possible, otherwise symptomless and rare occurrence of cyanosis.

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CONTRIBUTION TO THE STUDY OF GASTRIC TUBERCULOSIS*

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Cases of gastric tuberculosis have been so infrequently reported, that the addition of new cases is, we believe, of sufficient interest to warrant their recording. To the 367 cases collected by Clagett and Waltman[1] from the literature we can add now 10 cases observed in Greece. According to Chaffin[2] only 212 certified cases of this entity have been recorded until the time of his publication. Because of the propagation of gastrectomy in the last decades as a more radical treatment of peptic ulcer, it is probable that this will also lead to an increase in the number of observations of gastric tuberculosis. Until recently such cases were only rarely met in gastric operations. For instance, at the Mayo Clinic (1912-1915) only one case of tuberculosis was observed among 2,500 gastric operations, and Dehmel[3] reports only 3 cases among 1,568 similar operations. Sullivan, Francona, Kirschbaum[4] encountered 1 case of gastric tuberculosis, in a total of 75,000 various operations. It is possible, however, that many cases were not diagnosed, because either a palliative operation had been performed or the removed piece was not submitted to a histological examination. It is well known that the gross appearance of most tuberculous lesions of the stomach is not characteristic, so that it is difficult to distinguish them from the peptic ulcer and the carcinoma, without mentioning other rarer affections. Nevertheless, the occurrence of gastric tuberculosis will always remain a rare matter, as evidenced by its infrequency in autopsies. Kink and Rao[5] completed the statistical reports, collected by Melchior[6] and Mirolli[7]. These contain in total 81,217 autopsies with only 200 cases of gastric tuberculosis (statistics of Clayton-Wilkinson, Glaubitt[8], Gossmann[9], Grusden, Huebsmann, Orsos[10], Robertson, Ophuels, etc.) In a more recent study Sullivan et al report 2 cases of gastric tuberculosis observed among 11,480 autopsies. Even in autopsies of tuberculous subjects the incidence of gastric tuberculosis remains low. As seen from the collected reports of Eisenhard, Glaubitt, Gossmann, Hundrat, Letulle, Melchior, Plambeck, Simmonds, Ophuels, mentioned by Kink and Rao on 15,220 autopsies of tuberculous subjects only in 87 instances was a tuberculous lesion of the stomach demonstrated. Many explanations have been offered to account for this relative immunity of the stomach to the tuberculous infection. These are for instance, the germicidal action of the gastric juice, or the protection offered by the mucus[11], or the motility of the stomach[12], or the rarity of the lymphatic follicles in the stomach wall (Rokitansky), or the natural resistance of the gastric mucosa. Generally speaking the conditions in the stomach and the duodenum seem to be unfavorable for the establishment of the tuberculous lesion. When these conditions are modified, as for instance in cases of gastric cancer, tuberculous infection occurs more frequently, probably not only because of the

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existing achlorhydria and achylia, or the stagnation due to obstructive phenomena, or the associated gastritis, but also on account of the lessened resistance of the organism.

The first observations of gastric tuberculosis are credited to Louis 1825, Barkhausen 1828, etc. Later Cruveilhier 1842 and Lebert 1874, etc. contributed on the same subject. Litten 1876 and Talaman 1879 described the tubercles found in tuberculous ulcers of the stomach. After the discovery of the tubercle bacillus by Koch 1882, its presence in tuberculous gastric lesions was for the first time demonstrated by Coats 1887. Arloing 1902 experimentally reproduced tuberculous ulcers of the stomach by injection of tuberculous material in the blood stream. The tuberculous infection of the stomach can be primary or secondary. The primary is difficult to demonstrate and its existence has been contested by Aschoff[13] and Konjetzny[14]. According to Riedel[15] and Scacsway[16], only in 5 cases of gastric tuberculosis did the autopsy reveal no other visceral lesion. Few cases, about 15-20, have been described as primary, for the most part merely after clinical criteria (cases of Ruge[17], Luxemburg, Nollenberg, Rother[18], Alexander, van Wart, Nordmann, Biernath[19], Watson[20], etc.) But the exclusion of other associated tuberculous lesions is clinically almost impossible. For this reason the division proposed by Melchior[21] into surgical and nonsurgical cases has been more widely accepted. The surgical cases include the disputed primary lesions of the stomach, and those of the secondary ones with inactive or latent tuberculous foci. The nonsurgical cases are on the contrary those, in which occur active and progressive visceral lesions, principally of the lung and the digestive tube, so that the gastric location is only of minor importance.

The tuberculous infection of the stomach is occasioned either by ingestion of infected food, especially milk, or by deglutition of sputum containing tubercle bacilli, or through the bloodstream or along the lymphatics. Another source of infection is by the spreading of exogastric tuberculosis, as for instance, from the lymph nodes (Beneke) or the spleen (Reinhold) or the transverse colon, or the liver[22], etc., ulcerating through the stomach wall. This can lead to the establishment of a fistulous communication with the intestinal tube. Outside these infection sources other rarer ones are mentioned, as the propagation from the duodenum (Chiari), or from the peritoneum, or the retrograde transportation from the lymph glands into the gastric wall.

Gastric tuberculosis is usually divided into 3 forms, according to the division proposed by Leriche and Mouriquand[23]. These forms are the ulcerative, the hypertrophic and the sclerotic or scirrhous. Konjetzny distinguishes the following forms, the miliary, the ulcerative and the hypertrophic and Bianchi[24] the ulcerative, the hypertrophic, the infiltrating inflammatory, the nodular and the perigastric. If we set aside the miliary form, which only rarely is not a part of generalized tuberculosis and is therefore of little clinical interest, and if we unite in one form the hypertrophic and the scirrhous forms of Leriche and the hypertrophic, the infiltrating, perhaps also the nodular forms of Bianchi, we hope we can thus offer a satisfying compromise of the diverging views. Here we must also

discuss the assertion of Leriche, Mouriquand, Poncet[25], and other French authors, that a nonspecific inflammatory process leading to constriction, if situated near the pylorus, occurs by toxic influence proceeding from distant tuberculous foci. The tuberculous origin of this lesion has not been confirmed as yet and was, on the contrary, contested by other authors, as by Melchior.

The more frequent form is the ulcerative, which is often a part of widespread ulcerative process of the digestic tube or of ulcerative pulmonary tuberculosis[26]. Multiple tuberculous ulcers sometimes occur, as in the case of Willerding[27] where they amounted to twenty. The margin of the ulceration is frequently undermined and the floor covered by anemic granulations. Sometimes tubercles are evident. The size of the ulceration varies from a lentil to a palm. The ulcer is generally shallow and seldom penetrates beyond the submucosa. There is, therefore, little tendency to hemorrhage or perforation. Benjamin[28] collected from the literature 15 cases of severe hemorrhage from tuberculous ulcers with 6 deaths, and a case of perforation was recorded by Levy (1934). The seat of the ulcer is usually the pars pylorica and the lesser curvature of stomach, but frequently also the greater curvature is involved. The regional lymph glands are enlarged and sometimes contain caseous material.

The possibility that a simple peptic ulcer is infected by tuberculosis exists, but this is unusual[29]. On the other hand the infection of an ulcerated gastric carcinoma was repeatedly observed. Sprunt[30] collected 13 cases from the literature and many new ones have since been added[31] (Finsterer, Denk, Hajek, Baumgaertner-Bruns, Bolsakowa 1935, Deineka 1935, Bartolotti 1930, Tammann 1932, Luepke 1930, Tsunihisa 1930, Wolf 1930, Hurst 1930).

The hypertrophic form is usually mistaken for carcinoma, because in this form the other visceral tuberculous locations are little evident. The affected area of the stomach involves principally the submucosa which is replaced by a granulomatous infiltration. The muscular and the subperitoneal coat can also be involved, which leads to a fibrous thickening viscus and to constriction of the lumen. Scattered inside this fibrous tissue appear typical tubercles, containing lymphocytes, epithelioid cells and Langhans type giant cells. There is little tendency for caseation. The mucosa of the infiltrated area either shows a thickening of the folds and hyperemia, or becomes ulcerated. If the lesion is situated near the pylorus, this leads to a slowly progressive obstruction. The regional lymph glands along the greater and the lesser curvature are usually enlarged, and present typical tuberculous lesions. Sometimes they contain caseous material. Beside the aforementioned forms with many intermediates, other varieties have been described. Thus Becker[32] reports a case presenting a localized miliary tuberculosis of the gastric mucosa. Knofloch's and Pape's[33] case presented the appearance of a hypertrophic antral gastritis, without infiltration of the stomach wall. A case of tuberculous abscess in the wall of the pyloric antrum was published by Schlessinger[34], etc. Owing to the rarity of the entity, diagnosis is seldom possible before operation, or even before the microscopical examination of the removed viscus. In cases with active foci of visceral tuberculosis, the presence of a gastric ulceration

revealed by x-ray examination or a palpable gastric tumor can suggest the presence of a gastric tuberculosis. But the diagnosis in these cases affords little interest from the surgical standpoint. In cases however, in which the tuberculous lesion of the stomach is clinically the sole or at least the only apparent manifestation of tuberculosis, convincing clinical signs and laboratory tests are missing. The clinical diagnosis is likely then to be one of carcinoma or peptic ulcer. The differential diagnosis is likewise difficult from actinomycosis, syphilis, linitis plastica, hypertrophic antral gastritis and other rare diseases.

The clinical manifestations consist in abdominal pains aggravated after meals, nausea and vomiting of partly digested food. If the seat of the lesion is in the pars pylorica a progressive obstruction results and the patient soon becomes emaciated and dehydrated. Hematemesis and melena seldom occur. Blood is sometimes detected in the stool. The tuberculin test is of no great diagnostic value and its performance is not recommended, because according to Haberer[35], Tadaschi[36], Schlessinger, Curschmann, etc., the resulting focal reaction may lead to a perforation of the tuberculous ulcer. The roentgenologic examination is likewise not conclusive. According to the extent of the infiltrated area and the presence of an ulceration, diagnosis is made of a peptic ulcer or of a carcinoma. In case of multiple ulcers a tuberculous lesion can be suspected; likewise if the seat of the ulceration is along the greater curvature. The hypertrophic form usually suggests a neoplasm. Pyloric obstruction or hour-glass constriction in the middle of the organ, eventually a leather bottle aspect, with loss of peristalsis in the infiltrated area and filling defects are commonly demonstrated. The examination of the gastric juice after test meals gives inconstant results. The total acidity can remain normal, or is increased, but more frequently achlorhydria and achylia are found. The presence of tubercle bacilli in the gastric juice is rarely demonstrated and in case of associated pulmonary tuberculosis these can proceed from the deglutition of contaminated sputum. Only the microscopical examination of the removed specimen is conclusive, but even then it is not always possible to demonstrate the presence of acid fast bacilli in the sections. According to Groders only in 49 out of 167 cases of gastric tuberculosis was the presence of the tubercle bacilli demonstrated. Difficulties are occasionally encountered in the differentiation of the tuberculous from the syphilitic lesion, if tubercle bacilli or spirochetes, are not demonstrated at the microscopical examination and if the serological reaction is negative. Such cases have been reported by Barber, Beer, Colp and Heyd[37]. Therefore, the diagnosis of tuberculosis of the stomach on a morphological basis alone is always open to question. Still more questionable is the diagnosis if it is based only on the histological examination of a gland removed for biopsy, because it is possible that gastric carcinoma was secondarily infected by tubercle bacilli or that the presence of tuberculosis in the lymph nodes was only casual. The prognosis of gastric tuberculosis is not good, even if there is no evidence of another visceral tuberculosis. Only few cases have been reported as cured by internal treatment alone, and as a rule the lesion has the tendency to spread. The patient grows emaciated and dehydrated, on account of the pains and of the consequences of

pyloric obstruction. He soon becomes feverish and the lesion spreads to the adjacent organs or to the abdominal cavity, or generalization follows. At the same time the gastric lesion acts prejudicially on the course of the other tuberculous locations. For this reason operation in these cases is also indicated, excepting the more advanced ones. Of the surgically treated patients, a statistical analysis of Nieden[38] showed 57 per cent were cured. In particular, out of 49 treated cases, 28 cures followed, of which 14 were after gastroenterostomy and 14 after gastrectomy. As this last operation tends to become a typical proceeding for the treatment of peptic ulcers, it is probable that the results of surgical treatment in gastric tuberculosis will also improve. This is supported by the generally better results of the gastrectomies performed since 1927 for gastric tuberculosis. (Cases of Roepke 1927, Colp 1928, Hjort 1928, Barber 1931, Dax 1934, Scacsway 1934, Knofloch 1934, Watson-Flint 1936, Becker 1937, Kink-Rao 1938, Allessandri 1938, Gentile 1939, Chaffin 1939, Ganoli 1940, Sullivan 1940, Cortino 1941, etc.) Knofloch and Pape up until 1934 collected 58 cases of gastrectomy with 36 good results, and Gentile (1938) reports that of 21 more recent gastrectomies 15 were cured. Gastroenterostomy being only a palliative operation cannot be compared in the results with gastrectomy, because the remaining tuberculous lesion can spread in the surroundings. Mirolli (1929) reports that the mortality rate after 43 gastroenterostomies, not including the immediate postoperative mortality, amounted to 48 per cent, whereas after 24 gastrectomies this same mortality was only 11 per cent.

The following 10 cases were observed in Greece since 1927. Of these, 4 cases were published by Calogirou and Sophronis in the Greek periodical "Helliniki Iatriki", September 1927. The next 4 cases were recorded in the dissertation of Gabalas (Athens 1931). Lastly 2 cases have been presented before the Greek Society of Surgery (December 1946), the first by Christopoulos and the second by the present authors.

Our case report:—Female, 55 years old, married and mother of 4 healthy children. No family history of tuberculosis. Her father died of cancer of the stomach. The past history is not contributory. The present complaints date back about 3 months and consist principally of pains at the epigastrium, aggravated by the ingestion of food. Nausea, vomiting, hematemesis and melena are not recorded. Admitted at 22 September 1946.

Examination:—Patient is emaciated and anemic. Head, neck and chest are normal. A firm not movable mass, about 5 cm. in diameter, is palpated between the umbilicus and the right costal margin. There is some tenderness on pressure of the epigastrium.

Urine normal, blood count showed R.B.C. 3,400,000 and W.B.C. 6,800 and a normal differential count. The other laboratory tests were negative. Roentgenogram revealed an opaque area, about 3 cm. in diameter at the lesser curvature of the pyloric antrum, separated from the rest of the opaque stomach filling by a translucent halo. The roentgenogram appearances suggested an ulcerated malign

neoplasm. An x-ray examination of the chest demonstrated the presence of fibrous bands extending from the hilar region laterally and to the upper lobe. The right diaphragm is held high by adhesions.

Clinical diagnosis was gastric carcinoma.

Operation:—Under local infiltration the abdomen was opened through a high median incision. At the pars pylorica of the dilated stomach and principally in the posterior wall adjoining the lesser curvature, a hard tumorlike infiltration is palpated adherent to the pancreas. Enlarged lymph glands were felt along the lesser curvature. The mass was freed by blunt dissection from the pancreatic surface. Partial gastrectomy was performed after the method of Reichel-Polya. The enlarged lymph glands were removed. A drain was left on the denuded surface of the pancreas. Closure of the abdominal incision.

Postoperative course was uneventful. Discharged on the 12th postoperative day. Patient reported after the operation she is keeping in good health.

Pathologic report:—The ulceration is about 3 cm. in diameter, the margin is sinuous and slightly undermined, the floor is partly leved and partly granular covered by a thin whitish layer. The stomach wall adjoining the ulceration is infiltrated and thickened.

Histological examination:—A section taken from the base of the ulcer showed a granulomatous infiltration, principally of the submucosa, involving the superficial layers of the muscular coat. Scattered tubercle follicles are encountered principally near the margin, where they become confluent. The tubercle follicles contain epithelioid cells and numerous Langhans type giant cells. In other sections of the floor an inflammatory infiltration with polymorphonuclears lymphocytes and rare eosinophils occurs. Elsewhere there is a strong production of fibrous tissue, replacing locally the coats of the stomach wall.

Diagnosis:—Tuberculous ulcer of the stomach.

Comment:—In our case the clinical examination and the abdominal exploration did not reveal another active focus outside the gastric lesion. Nevertheless, it is not probable, on account of the patient's age, that the gastric lesion was the primary tuberculous focus. There is also no evidence that the infection has spread from the lymphatic glands to the stomach wall, because these show only recent tuberculous lesions. The possibility that the infection of the stomach is hemogenous certainly exists. Many authors, for instance Arloing, Patronicolas[39], Gabalas, etc., believe this mode of infection as the most probable, others such as Liebermeister, maintain that there is no evidence that this mode is the cause of the ulcerations of the peptic tube. Therefore, we are inclined to accept as more probable that a reinfection, conveyed by the food has occurred in our case.

The following 4 cases are taken from the report of Calogirou and Sophronis:

Case 1:—Male, 27 years old. No family history of tuberculosis. There is nothing of note, in the previous history. For the past 1½ years, he complains of periodically appearing pains at the epigastrium and when the stomach is empty. The ingestion of foods relieves the pains. About 4 months ago these symptoms

became aggravated. Nausea, acid eructations and vomiting of partly digested foods sometimes containing remnants of past meals were added. No hematemesis or melena is mentioned.

Examination:—Patient is thin and pale. Tenderness on pressure beneath the xiphoid and visible peristalsis of the stomach. Chest and other systems are normal. The gastric juice examined after test meal revealed achlorhydria and the presence of lactic acid. No blood was discovered in the stool. The blood count showed a slight anemia. The x-ray examination of the chest demonstrated a moderate opacity of both upper lobes and calcified hilar glands. At radiological examination of the stomach a pyloric stenosis was found and dilatation of the stomach.

Operation:—The stomach was covered with a fine layer of perigastric adhesions, principally at the pars pylorica. In this area an inflammatory infiltration of the wall could be palpated, about 2.5 cm. in extent, producing a notable obstruction. Enlarged lymph glands were palpated along the greater and lesser curvature.

The histological examination of a gland removed for biopsy demonstrated the presence of tubercles with giant cells.

Comment:—In this case the diagnosis of tuberculosis was based solely on the histological examination of a removed gland and remains of course open to question, all the more so as nothing is known as to how the patient has fared since his discharge.

Case 2:—A man of 22 years. In the past history nothing noticeable. For the past year and a half he complains of a sensation of fullness after meals, followed by nausea and pains above the umbilicus. The last 40 days he vomited 4-6 hours after meals material sometimes containing food, taken the previous days. Two hematemeses are mentioned.

Examination:—Patient is pale and emaciated. Clinical examination of the chest revealed an atelectasis of the right lower lobe. At the epigastrium a diffuse mass is palpable. The epigastrium is tender on pressure. Examination of the gastric juice showed achlorhydria and the presence of lactic acid. Stool examination for blood was positive. The radiological investigation of the chest revealed a moderate fibrosis in the right lower lobe. The x-ray examination of the stomach demonstrated a pyloric obstruction and the presence of a niche. The stomach was very dilated.

Operation:—A dilated stomach with hypertrophic walls appears. The pars pylorica is occupied by a firm inflammatory process. At the greater and the lesser curvature enlarged caseous glands were felt. The microscopical examination of one gland removed for biopsy demonstrated tuberculous lesions.

Comment:—The same remarks as in the first case.

Case 3:—Female, 18 years old. Her mother died of tuberculosis of the larynx. Past history nothing of note. For the last 14 months, she complains of slight pains, beginning 2 hours after meals and lasting for an hour. In course of time

the pains became aggravated and more continuous, followed by a burning sensation and sometimes by vomiting. Hematemesis and melena has thrice occurred.

Examination:—Emaciated and dehydrated patient. Lungs, liver, heart and kidneys normal. A slight tenderness is felt at palpation above the umbilicus. A splashing sound is heard on palpation of the epigastrium. Test meal demonstrated achlorhydria and the presence of lactic acid. No blood was detected at the examination of the stool. Radiologically the chest revealed nothing pathological. The x-ray examination of the stomach demonstrated a pyloric stenosis with an annular niche and gastric retention and dilatation.

Operation:—A greatly dilated stomach was seen. The pylorus and duodenum was fibrosed and the lumen partially obstructed. A partial gastric resection was performed. The histological examination demonstrated the presence of typical tubercles, principally situated in the submucosa.

Comment:—Because of the histological examination of the removed piece, the diagnosis of gastric tuberculosis, in this case seems certain, although the presence of tubercle bacilli was not demonstrated in the sections. Unfortunately the patient has not reported after her discharge.

Case 4:—Female, 45 years old. Past history noncontributory. A year before she complained of a sensation of fullness after meals, followed by acid eructations and later by pains beneath the xiphoid, 3 hours after ingestion of food. Sometimes copious vomiting of partly digested food followed.

Examination:—Patient is emaciated and anemic. Lungs, heart and nervous system were normal. A visible gastric peristalsis is observed. A firm mass is palpated above the umbilicus, which is very tender. An examination of the stomach revealed a mediocre dilatation, with a filling defect at the lesser curvature near the pylorus.

Operation:—Half of the greater curvature is occupied by a firm granulomatous tumor. Enlarged lymph nodes are palpated along the vertebral column and the omentum. A gland removed for biopsy demonstrated typical tubercles with giant cells.

Comment:—As a histological examination from the growth itself is missing, diagnosis remains questionable. Nothing is mentioned about the state of health of the patient after her discharge.

The authors maintain that the last two cases mentioned were primary. This is not very probable because a family tuberculosis is reported in the 3rd case, while the advanced age of the 4th case makes this supposition seem unlikely. With regard to the mode of infection, Calogirou and Sophronis believe, that in their first 2 cases which they regard as secondary, the viscus was invaded from the diseased lymph glands, by retrograde transportation.

A fifth case reported by the same authors, presenting an abcess in the submucosa of the pyloric antrum, with no histological evidence of tuberculosis, was not included in our present report.

Gabalas, in his dissertation (Athens 1931) has reported 4 cases of gastric tuberculosis from the pathological laboratory of the hospital.

With the exception of one, these cases have no surgical interest, because of the associated widespread visceral tuberculosis. For instance, at the first reported case, beside the gastric lesion, the postmortem examination demonstrated tuberculous processes in the liver, the omentum, the pericardium, both the lungs, the peribronchial glands, and the pleura. In the second case a miliary tuberculosis of the lungs, the liver, the kidneys, and the meninges was concomitant with a chronic tuberculosis of the intestines, the stomach, the abdominal lymph glands, the prostata and the epididymis. In the third case a tuberculosis of the peritoneum and the abdominal lymph glands had spread on the stomach and a caseous gland of the lesser curvature had ulcerated through the stomach wall. Associated with these lesions was a chronic tuberculosis of the lung with caseous hilar glands. The aforesaid cases appertained to the ulcerative form of gastric tuberculosis. The gastric lesion was in no case clinically diagnosed and only the postmortem examination demonstrated the gastric location. For these reasons we have withheld reporting the above cases in detail. The remaining 4th case is, on the other hand, clinically interesting.

Female, 27 years old. Past history is not contributory. A year before patient stated that she had slight pains at the epigastrium, appearing 1-2 hours after meals. A sensation of fullness, acid eructations and sometimes copious vomiting of sour tasting material followed. No hematemesis or melena has occurred.

Examination:—Patient is emaciated and pale. Chest, friction is heard over a small area at the right basis. Visible peristalsis of the stomach. At palpation of the abdomen a splashing sound is produced. Blood count R.B.C. 4,200,000, W.B.C. 6,000 with a normal differential count. Urinalysis. Traces of albumen, rare red bl. corp., slight cylindruria. Test meal showed free HCl 0.38 per cent, total acidity 0.70 per cent, traces of lactic acid. Blood urea normal. The x-ray examination of the stomach demonstrated a ptosis and dilatation of this organ, whole lower limit attains the pubic symphysis. Notable hypersecretion, diminished peristalsis. After 5 hours a small portion of the barium meal has left the stomach.

Operation:—Ether administered. High median incision of the abdomen. A greatly dilated stomach appears with very thickened walls. An inflammatory mass, the size of a goose egg occupies the pars pylorica. Enlarged and caseous lymph glands are palpated, along the lesser curvature. There are extensive adhesions between the growth, the pancreas and the ligamentum hepatoduodenale. On the gastric serosa a number of scattered nodules are seen, as large as a pea. The mass is freed by blunt dissection from the pancreas and the ligament. A partial resection after Reichel-Polya is performed. Closure of the abdomen.

The temperature rises to 38.5-39.5° C and the pulse to 140. Abdomen on palpation not tender. Mucopurulent expectoration. The state of the patient is progressively aggravating. The x-ray examination detected a collection of fluid

in the right subphrenic space. On the 12th postoperative day the patient succumbed.

Gross appearance of the specimen:—The gastric mucosa is moderately thickened. Near the pyloric antrum an extensive irregular exulceration is seen, with undermined margin and with the floor partially covered by hypertrophic granulations. At the site of the pylorus the ulceration is becoming annular. The stomach wall there is 1-1.5 cm. thick and produces a notable constriction. Along the greater and lesser curvature enlarged lymph glands are encountered.

Microscopical examination:—At the pars pylorica the mucosa is partially ulcerated and is substituted by an inflammatory granulomatous tissue. In the submucosa scattered tubercles with giant cells are demonstrated. Tubercles are also encountered between the muscular coats and the subserosa. The fibrous tissue in the stomach wall is very thickened and the muscular coat is hypertrophied. Disseminated lesions of chronic endarteritis obliterans are demonstrated.

The postmortem examination revealed that the death cause was an acute generalized peritonitis. Beside this area of bronchopneumonic consolidation were demonstrated in both lungs. Also tuberculous caseous glands at the hilus, principally of the right lung, at the porta hepatis and at the mesenterium.

Comment:—Author believes that the infection of the stomach occurred through the blood stream, probably from the tuberculous hilar glands, without excluding the possibility of infection through the lymphatics.

Case of Christopoulos:—The last case of gastric tuberculosis was presented by Christopoulos at the Greek Surgical Society, December 1946.

Admitted December 1936, at the hospital, Evangelismos, male, 39 years old. Thirteen years ago patient had a hemoptysis. The subsequent clinical examination did not reveal any pathological process in the lungs. Patient states that later, 5 years before admission, he felt a sensation of fullness after meals and besides this, during the week he had pains at the epigastrium and vomiting. Then for about 2 years he had no complaints. Two years ago once more gastric pains occurred periodically 2-3 hours after meals, followed by eructations and a burning sensation beneath the xiphoid. For the past 6 months these symptoms became aggravated and were sometimes followed by vomiting and by acid or foul smelling eructations. No hematemesis or melena was observed.

Examination:—Patient is emaciated and dehydrated. Chest: Crepitations heard at the basis of the right lung. The epigastrium is tender on pressure between the umbilicus and the xiphoid.

The laboratory examinations were normal.

At the radiological examination a notable pyloric obstruction was revealed with retention of the barium meal in the stomach.

Operation:—Nitrous oxide administered. The abdomen was opened through a high median incision. The pars pylorica was occupied by a firm growth the size of a big nut, suggesting a carcinoma. The regional lymph glands were not enlarged.

There were no adhesions to the neighboring organs. Partial gastrectomy was performed after Finsterer.

The postoperative course was normal in the first days. At the end of the first week the patient became feverish. The fever rose to 39° C and was followed by profuse perspiration. The x-ray examination of the chest revealed a recrudescence of the tuberculous process in the right lung. The patient was therefore transferred to a sanitarium, whence he was discharged after a year, greatly ameliorated.

The histological examination of the specimen demonstrated the presence of tuberculosis at the pars pylorica. Typical tubercles were scattered at the mucosa, submucosa and the muscular coat, containing giant cells and partially caseated. The regional lymph glands were normal.

Comment:—This histologically demonstrated case of gastric tuberculosis was surely secondary, because the pulmonary location, although not clinically verified at the beginning, preceded by many years the manifestation of the gastric lesion. The most probable modes of infection were either by the blood stream or by ingestion of contaminated sputum.

Conclusions

Tuberculosis of the stomach, though it is a rare disease, remains a subject of clinical interest, as is indicated by the number of papers written. It is even probable that this interest will increase in the future because the more cases of various gastric diseases that are submitted to gastrectomy, the more specimens will be available for histological examination and therefore fewer cases of gastric tuberculosis will be overlooked. The rarity of the entity and the absence of probational clinical and laboratory findings, will not permit, in most instances, an accurate diagnosis before surgery or even before the histological examination. According to these findings, of which the more weighty are the radiological ones, diagnosis is being made of peptic ulcer or carcinoma. This deficiency is, however, of minor importance as gastrectomy is at present the prevalent method of treatment of these diseases and likewise of the rarer gastric diseases such as actinomycosis, lymphogranuloma, syphilis, etc. Therefore, the timely diagnosis and the correct evaluation of the regularly associated tuberculous lesions of other organs is of greater importance, because on these depend the immediate and late postoperative results. Whenever the radical operation is contraindicated for local or general causes, a palliative operation, such as gastroenterostomy, can be performed, to alleviate the symptoms of pyloric stenosis and to raise the general condition of the patient. But gastroenterostomy is not to be compared as to results with gastrectomy, because of the possibility that the gastric lesion may spread to the neighboring organs and the abdominal cavity or generalize. However, even if a radical operation is performed the prognosis depends on the form tuberculosis of the stomach assumes. Thus the results of the surgical treatment in the hypertrophical form are better than those in the other forms, because in this form the coexisting tuberculous lesions are usually nonactive. More difficult is the choice of

treatment in cases with associated active systemic tuberculosis, on account of the difficulty of obtaining a successful treatment of these lesions. The gastric location of tuberculosis, with its sequels, achlorhydria and pyloric obstruction, by impeding the nutrition of the patient, acts prejudicially on the course of the other tuberculous lesions. For this reason, the removal of the diseased viscus must always be contemplated, whenever the general condition of the patient permits the performance of the operation without any undue risk. But on account of the limited experience of most surgeons to judge the severity of the associated visceral tuberculosis, in cases in which the nature of the gastric lesion is known, the collaboration with a specialist is to be recommended.

The report of cases observed and treated will also contribute to the better knowledge of the diseases and improve the results of the surgical treatment.

This was the purpose of the present paper.

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CHAPTER ACTIVITIES

Boston Chapter

At a recent meeting of the Boston Chapter of the National Gastroenterological Association, Dr. Newton C. Browder was elected President for the coming year.

Dr. Charles W. McClure remains Secretary-Treasurer.

The next meeting of the Chapter will be held on Wednesday evening, 15 February 1950, at the U. S. Marine Hospital.

Following a dinner at 6:30 p.m., through the kind hospitality of Capt. K. R. Nelson, Medical Officer in Charge, the scientific portion of the meeting will consist of presentation of cases of 1. Pancreatic Cysts, 2. Unusual Gastrointestinal Tract Bleeding under the auspices of the Surgical Chief, Howard D. Fishburn and his Associates and, 3. Esophageal Peptic Ulcer with Constriction, 4. Intestinal Hemorrhage in Typhoid Fever, by the Medical Chief, Wm. S. Baum and his associates.

New Jersey Chapter

A meeting of the New Jersey Chapter of the National Gastroenterological Association was held at the Jersey City Medical Center on 16 January 1950.

The scientific portion of the program consisted of a Symposium on Chronic Biliary Tract Disease. Dr. Benjamin J. Macchia spoke on the Clinical and Laboratory Aspects; Dr. Leonard Troast on the Roentgen Aspects; Dr. J. A. Riese on the Medical Aspects; Dr. Earl J Halligan on the Surgical Aspects; Dr. Irving Marshall presented Pre- and Postoperative Care and Dr. Kenneth Catlaw, Postcholecystectomy Sequela.

New York Chapter

The next regularly scheduled meeting of the New York Chapter of the National Gastroenterological Association will be at the New York Academy of Medicine on Monday evening 13 March 1950.

Dr. Anthony Bassler, Honorary President of the National Gastroenterological Association will present "A Case of Multiple Carcinoma of the Colon Complicated by Abdominal Abscess", which will be discussed by Dr. M. W. Mettenleiter, Attending Surgeon, St. Clare's Hospital.

Dr. Frank J. McGowan, Visiting Surgeon, St. Vincent's Hospital will present "Surgical Treatment of Recurrent Diverticulitis of the Sigmoid Colon" which will be discussed by Dr. Louis M. Rousselot, Director of Surgery, St. Vincent's Hospital and Dr. Miguel C. Elias, Attending Surgeon, Gouverneur Hospital.

The third paper of the evening will be presented by Dr. Franklin Hollander, Head of the Gastroenterology Research Laboratory, The Mt. Sinai Hospital, entitled "The Action of Eugenol on the Gastric Mucous Barrier—With Reference to its Use in Ulcer Therapy". The discusser will be Dr. Stewart Wolf, Associate Professor of Medicine, Cornell University Medical College.

Members of the New York Chapter and physicians in the New York area are cordially invited to attend.

The first clinical session of the Chapter will be held on Monday evening, 10 April 1950.

Dr. Franz J. Lust is chairman of the New York Chapter Program Committee.

NEWS NOTES

Second European Congress of National Associations of Gastroenterology

The Second European Congress of National Associations of Gastroenterology will be held in Madrid, Spain, 3-7 May 1950.

Dr. Heliodoro G. Mogena is President, and Dr. Damaso G. Arrese is General-Secretary.

The Provisional Program as received from the headquarters office states that the general topic to be discussed will be "Diseases of the Biliary Tract, Except Lithiasis and Cancer". The preliminary list of speakers follows: Physiology of the Biliary Tract, Professor Gregory of Liverpool; Pharmacology of the Biliary Tract, Dr. Revers of Utrecht; Biochemical Methods in the Differential Diagnosis of Biliary Obstructions, Professor Jimenez Diaz of Madrid; Functional Disorders of the Biliary Tract, Clinical, Radiomanometric and Pathological Study, Professors Chiray and Caroli of Paris; Clinical Diagnosis, Dr. Pavel of Bucharest; Treatment, Professor Mallet-Guy of Lyon, Professor Odin of Göteborg and Dr. Lagerlof of Stockholm; Noncalculous Cholecystitis and Cholangitis, Etiology and Pathogeny, Professor Kapp of Basilea; Clinical Study, Dr. Gallert Mones of Barcelona; Radiology, Professor Santos of Lisbon; Pathology, Professor Nicod of Lausanne; Treatment, Professor Hernando of Madrid and Dr. Douthwaithe of London; Biliary Fistulae, Professor Hellstrom of Stockholm; Congenital Anomalies of the Biliary Tract, Dr. Massion of Brussels; Benign Acquired Stenosis of the Biliary Tract, Professor Van Goidsenhoven of Louvain and Professor Appelmans of Louvain.

Those proposing to attend this Congress are requested to send their application to the General-Secretary, whose address is Jorge Juan, 41, Madrid, Spain no later than 1 March 1950.

The subscription rate for full membership and formal payment will be announced in due course.

All members will have the right to take part in the discussions and present papers on the general theme.

Members of the Congress and their families enrolled as Associate Members will be invited to visit Toledo and El Escorial in a group excursion arranged by the Organizing Committee.

The Ladies Committee has arranged a program for the Ladies including visits to museums and artistic monuments. A farewell banquet will be given to all members of the Congress.

Correction

In the article "Corticodiencephalic Gastrointestinal Syndromes in Epileptics", which appeared in the January, 1950 issue, the illustrations appearing on pages 33 and 35 were incorrectly numbered. The illustration appearing on page 35 should have been Figure 4 and that on page 33 should have been Figure 5.

In Memoriam

We record with profound sorrow the passing of Dr. Manly Finkelstein, Member, Winnipeg, Canada.

We extend our deepest sympathies to the bereaved family.

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ABSTRACTS

GASTROINTESTINAL TRACT

PRACTICAL NUTRITION OF THE GERIATRIC PATIENT. Joseph L. De Courcey. Geriatrics. 3:353, (Dec.), 1948.

The author discusses the practical problems of 24 surgical and 14 nonsurgical cases of the aged—ranging from 50-86 years. In advanced life the wasting of tissues and organs produces a decrease in N content of muscles, due to protein loss.

The cases were fed a specially formulated powdered milk, Gerilac, fortified with Vitamin A and minerals. This is a spray-dried mixture of whole milk, skim milk, dried brewer's yeast, fortified with riboflavin concentrate, ergosterol, ascorbic acid, niacinamid, monocalcium phosphate and iron citrate, which provides a high protein and low fat content.

In a period of 2 weeks to 3 months they were given two eight ounce glasses of Gerilac daily as a supplement. This was found to be quite palatable, readily digestible and well tolerated. Clinical improvement was evidenced by gain in strength, better appetite and gain in weight, increase in hemoglobin, R.B.C. and W.B.C. return to normal. A sense of well-being accompanied all cases.

LOUIS K. MORGANSTEIN

PROBLEMS IN GASTROINTESTINAL SURGERY AS AFFECTED BY ADVANCED AGE. John T. Reynolds. Geriatrics. 4:161, (June), 1949.

Advanced age is no deterrent to necessary surgery. Two factors must be kept in mind in surgery of the aged. First, the rate of healing slows as age advances. Secondly, complications which appear minor or may go unrecognized in younger persons may be very disastrous in the aged. All complications must be anticipated preoperatively to be effectively avoided, and postoperative care must be of the very best.

Preoperative care, especially in gastrointestinal surgery, must include systemic care. No disease must be present—such as diabetes, T.B., etc. An internist and urologist should be in attendance. Pulmonary care should include oral hygiene, the emptying of the tracheo-broncheal tree, and the preoperative use of penicillin aerosol or parenterally as a prophylactic. In urologic complications one must consider prostatic disease with bladder retention. Postoperative catheterization should be avoided and the patient allowed to leave the bed to urinate. If it becomes necessary, strict sterile technic as well as a minimum of trauma is most important. As to vascular complications, the danger of thrombophlebitis and pulmonary emboli is great. Prophylactic femoral vein ligation should be considered if the operative and postoperative period should be long and shocking. Anticoagulant therapy is not considered wise, especially in operations on the rectum and esophagus, where you have large operative surfaces after the operation.

Local care of the G.I. tract should include and aim at the following:

1. Relief of obstruction. 2. Sterilization of fecal material. 3. Liquefaction and reduction of bulk.

LOUIS K. MORGANSTEIN

THE MECHANISM OF GASTROINTESTINAL ROENTGENOGRAPHY. George H. Stein and Manfred Kraemer. J. M. Soc. New Jersey. 45:539, (Nov.), 1948.

The purpose of this article is to acquaint those specializing in x-ray of the digestive tract with the needs, proper type of equipment, proper preparation of the patient, proper methods of examination, etc.

In choosing equipment the outfit should be shock-proof and sufficiently powerful to penetrate an obese abdomen of 200 pounds. This means at least a 200 milliampere apparatus with a movable Bucky diaphragm under the table. A tilt table is more or less necessary for horizontal and vertical fluoroscopy, and it is well to have two x-ray tubes, one over the table and one under the table. Ventilation of x-ray and dark-room should be provided.

Spot films of lesions or suspicious shadows seen during fluoroscopy are important and make for better diagnosis. The dark-room tanks should not be too small and solutions should be kept at proper temperature. The room should be fairly large and should allow for shelves, cabinets, dryers, etc. Smoking should not be permitted and room should be kept clean.

As to hazards and safety factors, gloves and apron are a must. Eyes should be accommodated before fluoroscoping patient, allowing use of less m.a. and k.v.p. which is an added safety factor. A minimum of 20 minutes of dark adaptation goggles is essential. The harmful effects are leukemia, skin changes from excessive exposure without protection, as well as glandular, skeletal and fetal deformities. The maximum tolerance dose is 0.05R to 0.1R in a 24 hour period. The authors use a Victoreen manometer, which they describe in detail, to detect and measure stray radiation. They also suggest the taking of blood counts at least every three months on personnel using x-ray equipment.

The patient must fast at least 8 hours prior to examination. In obstruction, preliminary gastric lavage is advised.

The authors then go into great detail of technic in examining patients during fluoroscopy, enumerating various things to do and look for, proper positioning of patient, etc. They also stress the necessity of taking films in the various outlined positions. For small bowel studies the patient is given one-half glass of thick barium mixture, fluoroscoped, and filmed at hourly intervals until stomach is empty. After the stomach is empty, the patient has a light lunch. One hour later and every hour thereafter films are taken until the head of the barium meal is in the colon and the tail is in the terminal ileum. It may be necessary to take films for 15 hours after ingestion of barium in order to obtain satisfactory views of terminal ileum.

For barium enema examination a printed instruction card is given the patient as to how to take the enemas. Prior to examination the patient is reassured that it is painless and that he will be given a chance to evacuate his bowel as soon as films are taken. Accidents should be expected and be provided for. Barium is allowed to flow in and the colon is visualized in all positions fluoroscopically. Films are then taken. Speed is important and after evacuation more films are taken.

The authors start every x-ray examination of the G.I. tract with a cholecystogram. The previous evening the patient is given Priodax, one tablet for every 25 pounds of weight, together with an instruction card as to proper procedure for preparation, etc. At 8 A.M. the following morning films are taken and if a satisfactory view is obtained, gastric analysis is made, lasting from 8:30 to 9:30. After the stomach is empty, examination is performed as outlined previously. Next day a barium enema examination is done and if the previous gallbladder films were not satisfactory, a second dose of the dye is given and cholecystogram is repeated on the morning of the barium enema. Thus a cholecystogram, gastric analysis, gastrointestinal series and a barium enema can be completed in two mornings.

LOUIS K. MORGANSTEIN

ESOPHAGUS

PEPTIC ULCER OF THE ESOPHAGUS WITH SEVERE BLEEDING CONTROLLED BY OXYCEL. Kenneth B. Castleton and David A. Dolowitz. Gastroenterology. 10:797, (May), 1948.

Peptic ulcer of the lower end of the esophagus probably occurs more commonly than has been generally suspected. A case is reported of bleeding esophageal ulcer in which the artery was observed through the esophagoscope. The hemorrhage was so severe that preoperative transfusions of 2,500 cc. of blood did not prevent the patient from being virtually exsanguinated. Oxycel applied topically was successful in controlling the hemorrhage. Subtotal gastric resection had been performed in the mistaken belief that bleeding was gastric or duodenal in origin. It is suggested that in cases where diagnosis is uncertain preoperative esophagoscopy may be of value. It is suggested that local application of oxycel may be used to control bleeding from esophageal varices as well as from ulcers.

FRANZ J. LUST

STOMACH

ON EFFECT OF HYDROCHLORIC ACID UPON GASTRIC AND DUODENAL MOTILITY. P. Brummer and A. Bundul. Ann. med. int. Fenniae. 38:1-4, 1949.

The authors studied the motility of the stomach and duodenum and the immediate effects of ingestion and also intragastric injections of two ml. of 10 per cent hydrochloric acid and then 200 ml. N/10 hydrochloric acid respectively. Twenty-nine subjects with a total of fifty examinations were carried out. Thirteen of the subjects were cases of insulin-proved achlorhydria and six of the remaining patients with acid gastric secretion had peptic ulcers. The studies were carried out via x-ray with the assumption that the contrast media had no special influence on the motility.

They concluded that the method of administration of the acid did not influence the effects on motility and that the effects are, therefore, probably produced by direct irritation of the stomach and duodenum. "An adequate dosage of the acid was found to cause cessation of both the gastric and duodenal peristalsis and a rise in the tonus". This was particularly true in achlorhydria cases and in those where free hydrochloric acid was not found in the empty stomach, but were not insulin-proved achlorhydria. The reason for using the intragastric injection method was to determine whether or not the effect of the hydrochloric acid on the motility might not be a secondary reaction resulting from the acid's irritation of the pharyngeal and esophageal mucosa. This was ultimately ruled out.

A. X. ROSSIEN

INTESTINES

SMALL INTESTINAL DEFICIENCY PATTERN: CURRENT STATUS. W. H. Glass. Am. J. Digest. Dis. 15:294, (Sept.), 1948.

Idiopathic steatorrhea and the disordered motor function of the small intestines (if it be on the same basis) respond to B-Complex therapy. Depending on the intensity of the illness, other

therapeutic measures such as dietary alteration to give adequate caloric intake of assimilable foods, Vitamin D in non-fat vehicle, and parenteral calcium, if an insufficient amount is absorbed, are, of course, indicated. The basic disease, however, is the alteration of the jejunal mucosa by deficient intake of some factor or factors in the whole B-Complex. Other therapy is indicated to treat the bodily changes subsequent to the altered absorption of intestinal content.

Grossly visible steatorrhea only occurs where there is extensive fat and soap content in the stool. In cases studied here, all who demonstrated significant mucosal changes in the jejunum, presented steatorrhea on chemical analysis of the stool. It is concluded that idiopathic steatorrhea is the more advanced phase of so-called B-Complex deficiency pattern. This latter term should no longer be used and Golden's terminology of Disordered Motor Function with a subdivision as to the etiological basis is much the preferred terminology. FRANZ J. LUST

ON THE RELATION BETWEEN GASTRIC SECRETION AND ROENTGENOLOGIC GAS CONTENT OF THE COLON. P. Brummer and A. Bundul. Ann. med. int. Fenniae. 38:5-8, 1949.

A study was carried out on 85 persons to determine the relationship between gastric secretion and the gas content of the colon as seen on x-ray. None of these patients had any proven organic diseases. Twenty-one of the subjects were insulin-proved achlorhydria, twelve had incomplete achlorhydria and fifty-two had normal or increased free hydrochloric acid.

The degree of gaseous content of the colon on x-ray films was evaluated in terms of 1, 2 and 3 with the first degree being the slight amount of gas. It was found that there is no difference in the gas content of the colon as observed on x-ray between achlorhydria and those patients having free hydrochloric acid.

The authors concluded "that no significant disturbances are to be seen in the bacterial flora of the colon in achlorhydria". A. X. ROSSIEN

PATHOLOGY AND LABORATORY RESEARCH

NOTES ON THE ELECTRON MICROSCOPY OF TISSUE SECTIONS. I. NORMAL TISSUE. II. NEOPLASTIC TISSUE. Albert E. Gessler; Clifford E. Grey; Mary C. Schuster; John J. Kelch and Maurice N. Richter. Cancer Research. 8:534-573, (Nov.), 1949.

Methods of sectioning, for the electron microscope, by the high speed microtome to the thickness of the order of 1/10 of 1 micron have been developed, as well as auxiliary technics of fixing and embedding of specimens, to produce electron micrographs possessing satisfactory detail with a minimum of distortion by coagulation and shrinkage. These methods have been employed for the investigation by the electron microscope of sections of normal animal and human tissue. Greater detail in general and some observations in particular have been presented by this method which are not revealed by the light microscope, since dimensions are often involved which are below the instrument's threshold of resolution. Consistently, the outer and nuclear membranes in the normal appear as firm and well defined boundaries. The nuclei are generally well formed with fine granular texture and much denser nucleoli. The cytoplasm seems to be characterized by a coarser background with well defined and denser granular particles while the intercellular tissue shows a submicroscopic fibrillar structure.

In neoplastic tissue sections, however, signs of aberration were observed. They seem to begin with the appearance of large numbers of vacuoles in intercellular tissue and cells. A characteristic aberration seems to be the breaking or disappearing of nuclear membranes and subsequent shrinking or breaking of the nuclear mass into dense fragments. A similar breaking of the outer cellular membranes frequently goes hand in hand, accompanied by the appearance of fibrils replacing them and often filling the cell interior. Every precaution has been taken to use only portions of tumors believed to be viable. The authors believe that some of the phenomena are signs of neoplasia. FRANZ J. LUST

LIVER AND BILIARY TRACT

THE SURGICAL GALLBLADDER. Victor B. Seidler. J. M. Soc. New Jersey. 46:10, (Jan.), 1949.

The author reviews 200 cases of gallbladder operations. Age incidence ranged from 20-79. One case was four and a half and another was 9 years old. From 31-60 there were 72 per cent. Seventy-nine per cent of the cases were women and there was a mortality of 5 per cent in those over 50 and only 1.3 per cent in those under 50.

The route of infection was either through the blood stream, biliary system or lymphatics. The types of inflammation were acute catarrhal, chronic catarrhal and advanced chronic inflammation. In this latter type, stones were most frequent. X-ray showed stones in 62 per cent of the cases. Non-functioning gallbladder in 19 per cent and no stones in 14 per cent where stones were found on operation. X-ray diagnosis was correct in 97 per cent of cases.

The symptoms involved pain in 90 per cent of the cases. Nausea in 47 per cent, and vomiting in 41 per cent.

Surgery should not be considered where visualization is poor and no stones visible unless:

1. All other factors capable of causing symptoms have been ruled out.
2. Patient is suffering from so much pain that cholecystectomy must be done for relief.
3. Abnormality of the biliary tract on two cholecystograms at intervals of a few weeks.
4. Medical treatment has been ineffective in relieving symptoms.

Surgery during attack and in the presence of inflammation is advisable as the organ can be easily removed, adhesions have not formed as yet, and the duct is closed so that gallbladder function is inhibited. Cholecystostomy should be done only if the patient is too ill, or if on exposing the organ it is found too difficult or too hazardous to remove. In the author's series 30 per cent had appendectomy done at the same time. Abdominal drainage was instituted in 88 per cent, common duct stones were present in 16 per cent and he explored it routinely in all cases. As to coronary disease 24 per cent gave history of anginal pains. True coronary was definitely diagnosed in 6 per cent.

The author lost only 6 cases and the average hospital stay was 11 days. LOUIS K. MORGANSTEIN

THE PROGNOSIS AND TREATMENT OF HEPATIC INSUFFICIENCY. Cecil James Watson. Ann. Int. Med. 31:405-423, (Sept.), 1949.

The author defines hepatic insufficiency as that state in which the patient's normal economy and activity is seriously interfered with because of a diffuse hepatic injury. In other words, a state in which the functions of the liver are unable to meet the general needs of the individual.

Prognosis and treatment of hepatic insufficiency are most difficult to evaluate. "Our ability to prognosticate or to treat liver disease on any rational basis, has made but tedious and small progress in the intervening centuries"—from the Hippocratic era to the present. This statement from an experienced clinician like Watson—should be a source of disappointment and embarrassment to all the ultra-scientific specialists and investigators who have given so much time and labor to the development of a long list of liver-function tests and their many modifications, including liver biopsy, turbidity tests, cephalin-cholesterol tests, dye tests, etc., etc. Perhaps, the "basic sciences", and the ever increasing numbers of tests of all kinds, and the many types and forms of precisional methods—and the use of various instruments of precision—are dulling our clinical judgement, and, all too often, are sources of confusion rather than clarification in some of our cases! The author quotes freely from the English translation of the works of Hippocrates (460-370 B.C.). The author advises that "a keen watch should be kept for the slightest sign of undue somnolence, disorientation, or euphoria, since these are often the first and ominous harbingers of hepatic coma. He emphasizes the "fetor hepaticus", "liver breath", or "amine odor", which means hepatic insufficiency even though jaundice may be slight or absent. He refers to palmar erythema, multiple-spider-nevi, recent loss of axillary hair, gynecomastia, venous collateral circulation and hemorrhagic tendency, either latent or manifest. The size of the liver is often of the utmost significance in prognosis. Rapid diminution in size is one of the most ominous signs of all indicating diffuse necrosis, and, as a rule, a fatal outcome with some exceptions.

Hepatic enlargement due to fatty metamorphosis or fatty cirrhosis, has a good prognosis.

The younger physicians of today are exceptionally well trained in the basic sciences and in the many newer tests and various technical laboratory procedures but, are they well trained today in the use of their senses of smell, taste, in keen vision and good hearing and careful palpation and percussion? Are they now developing their minds to the end that they have good clinical bedside judgement? Are they placing the proper weight and values of the many tests as against good clinical judgement? Dr. Watson properly emphasizes the importance of careful clinical observation including the value of the lost and discarded sense of "smell". How well the experienced clinician recalls the value of "smell" in cases of diabetic coma, uremia, rheumatic fever, typhoid fever, alcoholism, hepatic coma, certain forms of poisoning, etc., etc.!

The author discusses the value of diet and total-food intake, the value of glucose intravenously administered, preferably with some insulin to promote the appetite. The author cites an illustrative case of recovery from "alcoholic" cirrhosis. He used, advantageously, in some cases, frequent feedings of an enriched milk mixture on hourly schedule. He used chiefly Dietene Corporation's "Meritene"—a calcium caseinate—skim milk powder-lactose combination—which in certain individuals produces a tendency to diarrhea. Prognosis in cases of so-called "alcoholic" cirrhosis, is related to the degree of portal fibrosis, bile duct proliferation and adenoma formation with resulting shrinking and distortion of normal liver parenchyma.

The author refers to the use of intraheptol, liver extract, Vitamin B-complex, yeast powder, cholin-cystin mixture, and to Patek's use of diet plus yeast and B-complex, and to the work of Jones and Volwiler and Buck. Nine cases are cited in the article illustrating various types of hepatic insufficiency. The author closes by citing Adamson's paper on "The Liver as the Organ of Sanguification" referring to Thomas Bartholin and to Galen. Galen speaks of the liver as the all important blood-making organ and, that, if the liver is diseased, its function is also vitiated or disturbed.

HYMAN I. GOLDSTEIN

NONICTERIC HEPATITIS SIMULATING GRIPPE. Harvey E. Nussbaum and Edward N. Comando. J. M. Soc. New Jersey. 46:114, (Mar.), 1949.

The author cites cases seen during the winter of 1948. These were variously diagnosed as grippe, intermittent flu, or virus X, involving slight hepatomegaly and liver dysfunction evidenced by laboratory tests. For this test the author used the Methylene Blue test as described by Myers, consisting of adding .25 per cent of aqueous solution Methylene Blue Chloride to 5 cc. of urine drop by drop. If a green color develops and persists after 3 drops, but turns blue after 4 drops the test is mildly positive. If green color persists after 4 drops, the test is definitely positive. In suspicious and positive cases, other liver function tests were done—thymol turbidity, bromsulfalein, icterus index, cephalin flocculation, etc.

Early symptoms were faintness, vertigo, severe upper abdominal pains, radiating to the right subscapular region, malaise and aching muscles. Later symptoms, diarrhea and nausea. The liver was palpable in about half of the cases, but there was no splenomegaly. There was tenderness in R.U.Q., absence of lymphadenopathy, and fever was not marked. No patient developed clinical icterus, and icterus index varied from 6-16.

The author then cites 6 cases to illustrate the above. Nonicteric hepatitis is infectious from a public health standpoint as it can develop into an epidemic of the icteric form. This is also important from a morbidity standpoint as some patients do not return to complete normal liver function for several months. The long range effects of this disease have yet to be determined.

LOUIS K. MORGANSTEIN

INFECTIOUS HEPATITIS AND LIVER FUNCTION. Max Magnes. J. M. Soc. New Jersey. 45:580, (Dec.), 1948.

The author cites a series of 60 army cases. All had jaundice, all had received Yellow Fever vaccine and all showed up 2-4 months after administration of the vaccine. Later this vaccine was found to be contaminated, and after its correction, fewer cases occurred. Other factors predisposing to hepatitis were malnutrition, fatigue, and high incidence of upper respiratory infection.

The cause is a filtrable virus which is present in stool and blood of infected persons and thus transmitted. Transmission may also be by syringe, needle, etc. Incubation period may be from 15-45 days. The pathology is that of liver damage of a hepatocellular type. There is marked mononuclear cell infiltration of the periportal area with mild infiltration of the intralobar area. This infiltration consists of macrophages, lymphocytes and a few eosinophiles and polymorphonuclear leucocytes. In the portal type there is widespread necrosis with lysis of the cells. In the nonportal type the liver cells show changes from cloudy swelling to definite necrosis. The bile capillaries may be blocked or destroyed. In liver biopsy studies, maximum changes occurred one week after onset, while after a month the changes were mild to moderate.

LOUIS K. MORGANSTEIN

BOOK REVIEWS

GYNECOLOGIC DIAGNOSIS. Robert Tauber, M.D., F.A.C.S., F.I.C.S., Associate in Gynecology and Obstetrics, The Graduate School of Medicine, University of Pennsylvania. 275 pages. Thomas Nelson & Sons, New York, 1949. Price $5.00.

The author aptly begins his introduction with the statement that: "Correct diagnosis is the basis of correct treatment".

Dr. Tauber's compact informative book aims to combat blind, uncertain, careless treatment and attempts to present modern step-by-step systematic approach to the correct diagnosis of pelvic disorders. Emphasis is placed on a careful history—as the first step toward a final correct diagnosis. Interpretation of the history—the previous complaints and diseases and the present symptoms and complaints are of great importance.

Careful consideration is given by the author to the physical examination (56 pages), to laboratory tests, diagnostic surgery, errors in diagnosis, and their prevention. The author includes a diagnostic clinic of case histories with examinations and diagnosis (170 pages). This unusual volume is highly recommended for students, internes, residents, and general practitioners interested in gynecologic and obstetric problems.

CLINICAL INTERPRETATION OF LABORATORY TESTS. Raymond H. Goodale, M.D., Pathologist at the Worcester City Hospital, Worcester Hahnemann Hospital, Belmont Hospital, and Fairlawn Hospital, Worcester, Mass., Clinton Hospital, Clinton, Harrington Hospital, Southbridge, Consulting Pathologist Veterans Memorial Hospital, Rutland Heights. 605 pages, 107 illustrations, 3 in color. F. A. Davis Company, Philadelphia, Pa., 1949. Price $6.50.

This excellent compact volume is a ready source for information on interpretation of laboratory tests—one of the best smaller books now available—for all medical students, internes, residents, and general practitioners. In this volume, the author adequately and concisely covers hematology, blood chemistry, serology, physiology of urine formation, and various tests of importance—including urea-clearance test, phenosulfonphthalein test, and Fishberg's test.

In Chapter 5 the author discusses physiology of the stomach including consideration of the normal gastric contents and the abnormal findings in gastric contents, duodenal contents, normal and abnormal, and, in Chapter 13, consideration is given to bacteriological examination of gastric and duodenal contents. Cerebrospinal fluid, sputum, feces, spermatozoa, basal metabolic rate, liver and biliary function tests, bacteriological examinations (Chapter 13), rikettsias and viruses (Chapter 14), mycological examinations, skin tests, toxicologic examinations, endocrinologic tests, parasitic infections, metabolic diseases, and vitamin deficiencies are all discussed in Dr. Goodale's work.

This book is enthusiastically recommended for all medical students, internes, residents, and general practitioners, and also medical technicians.

DISCOVERERS FOR MEDICINE. William H. Woglom, M.D., Yale University Press, London. 229 pages. Oxford Press, 1949. Price $3.75.

The reviewer found this book most interesting to read. The introduction was well written and contains much informative historical material gathered by the able author from his extensive reading and accumulated knowledge of medical history.

In Chapter II, "Blood Pressure" is presented interestingly from the time of the Rev. Doctor Stephen Hales, Vierordt, Poiseuille, and Riva-Rocci. The work of Stephen Hales is thoroughly discussed in these 18 pages. "Respiration" (Chapter III) contains references to Hippocrates, Galen, Michael Servetus, William Harvey, R. Boyle and Robert Hooke. References are made to Richard Lower, John Mayow (1643-1679), Georg Ernst Stahl of Halle, Joseph Black and J. B. Van Helmont, Joseph Priestly; Antoine Laurent Lavoisier the founder of modern chemistry, Joseph Louis Lagrange, Astronomer and Mathematician, Hassenfratz and Cesar Legallois are not overlooked by the author.

Foxglove, is well presented in Chapter IV. Reference is here made to Silas Marner (George Eliot) and his knowledge of the value of digitalis (foxglove) in dropsy, and thus Sally Oates was relieved of her distress and dropsy. Of course, the author discusses the pioneer work of William Withering of Shropshire, as he lay dying a friend exclaimed "The flower of English medicine is WITHERING".

"Vaccination" is covered in 23 pages (Chapter V). Macaulay's reference to this filthy disease (smallpox)—is mentioned, in describing the death of the young and blooming Mary II, Queen of England, and consort of William III. Louis XV, of France, and probably Marcus Aurelius Caesar (according to Osler) died of smallpox. Jenner's work is discussed. The "Laryngeal Mirror"

contains early historical references from the time of the ruins of Pompeii (79 A.D.), India, and the Talmud, and Venice of 1587, is mentioned. Borell's concave mirror, Archibald Cleland's apparatus, Bozzini of Frankfort, Benjamin Babington's Glottiscope, Cagniard de la Tour's Mirror (1825), Selligue's laryngoscope, Bennait (1832), Baume's (1838) mirror, Avery's laryngoscope, and Manuel Garcia a singing teacher of London all receive mention. Garcia's work is quite well discussed.

The author presents interesting historical data on "The Eustachian Tube" (Chapter VII)—with references to Monsieur Edmé Gilles Guyot (1724) postmaster at Versailles, J. G. du Verney (1683), and Wathen's catheterization of the Eustachian Tube.

"Eyeglasses and Spectacles" (Chapter VIII), "The Itch" (Chapter IX), "Quinine", "Phagocytosis", "X-Rays", "Heredity" (Mendel), "Milk Sickness" and an excellent bibliography complete this highly recommended addition to medical history.

All students, and physicians, will enjoy reading this book—yes, and the cultured laymen too.

THE DIAGNOSIS OF PANCREATIC DISEASE. Louis Bauman, M.D., foreword by Allen O. Whipple, M.D. 74 pages. J. B. Lippincott Company, Philadelphia, Pa., 1948. Price $5.00.

Although only a small volume of 74 pages, Dr. Bauman covered the subject of pancreatic function tests and their interpretation in various conditions.

With the great amount of material at his command at the Presbyterian Hospital, New York City, the author was able to check his findings at the operating table and at autopsy.

The difference in the quantity and quality and permanent concentration of the pancreatic secretion evoked after secretion injection as compared to that of mecholyl is interesting.

The serum amylase elevation may be due to causes other than pancreatitis or common duct obstruction, as the reader may note from Dr. Bauman's observations.

This volume is recommended to clinicians as well as surgeons.

THE EPITOME OF ANDREAS VESALIUS. Translated from the Latin with Preface and Introduction. L. R. Lind, Ph.D., University of Kansas, Anatomical notes, C. W. Asling, M.D., Ph.D., University of California, foreword, Late Logan Clendening, M.D. 103 pages and 25 pages of the Latin Text. The Macmillan Company, New York, 1949. Price $7.50.

All medical historians, book collectors, students and physicians everywhere will want this splendid work for their library.

Doctors Lind, Tracy and Asling deserve the thanks of the profession for this fine piece of work.

This translated Vesalius' "Epitome" will be an "admired" companion—addition to the forthcoming English translation by Professor J. B. de C. M. Saunders and Charles D. O'Malley of Vesalius *de Humani Corporis Fabrica Libri Septem* (1543).

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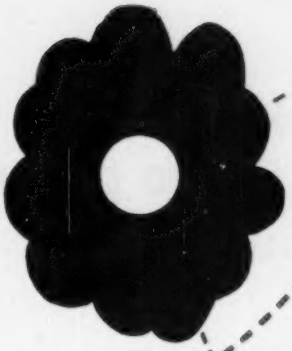

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[1]Kraemer, M.: Postgrad. Med. 2:431 (Dec.) 1947.
[2]Kraemer, M., and Siegel, L. H.: Arch. Surg. 56:318 (Mar.) 1948.
[3]Martin, G. J., and Wilkinson, J.: Gastroenterology 6:315 (Apr.) 1946.

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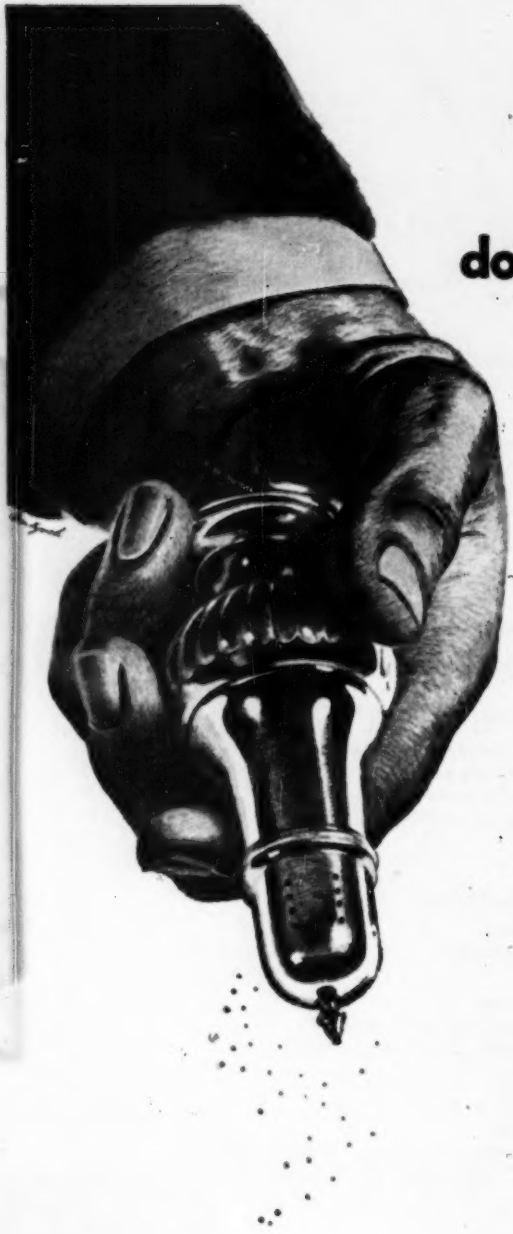

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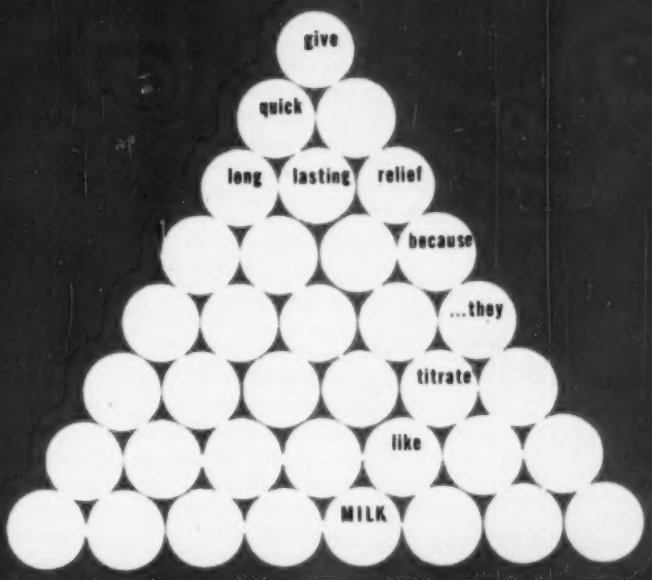

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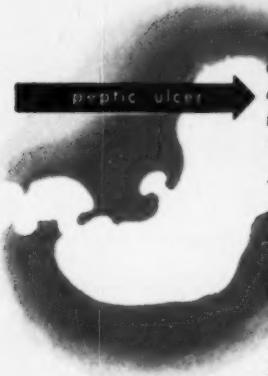

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Hubacher, O., Lancet,* ***251**, 272 (1946).*

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*Rivers, A. D., Am. J. Dig. Dis., **2**, 189 (1935).

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Gill, A. M., Lancet,* ***2**, (1945).*

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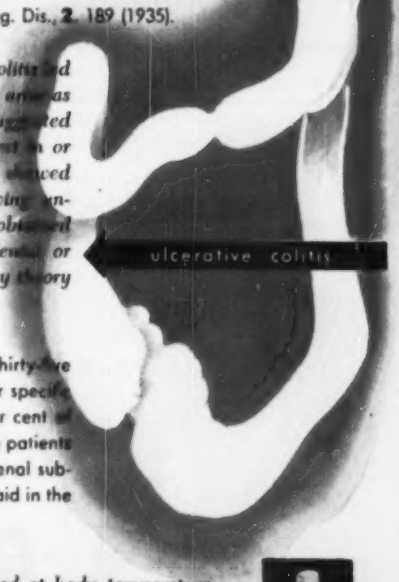
*Streicher, M. H., J. Lab. Clin. Med., **33**, 1633 (1948).



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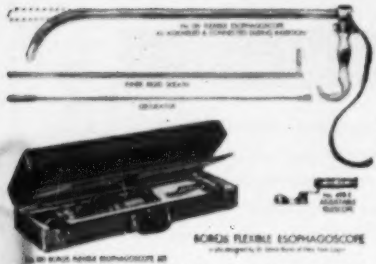

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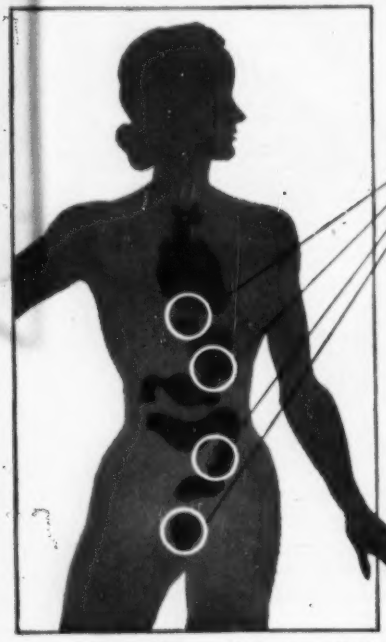

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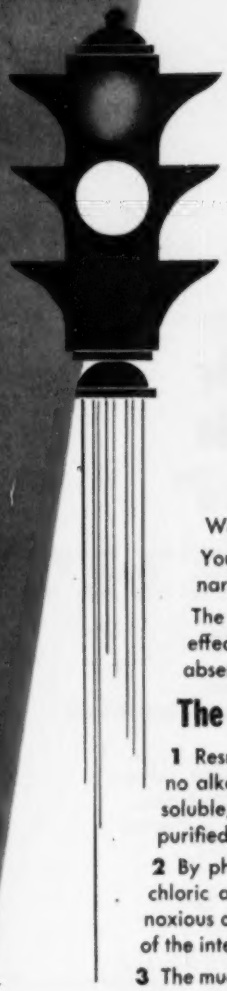

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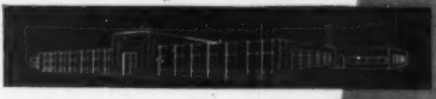

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*Wilbur, D. L.: Principles in the Use of Vitamins in Treatment: I. Vitamin Deficiency Diseases. Gastroenterology, 1:179, Feb., 1943.

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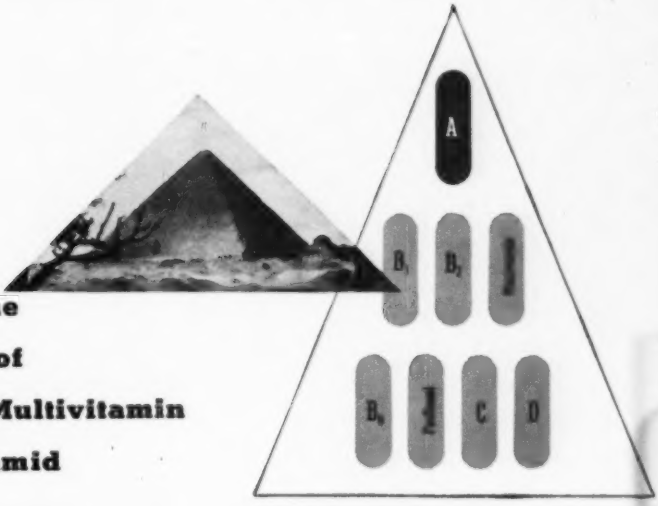

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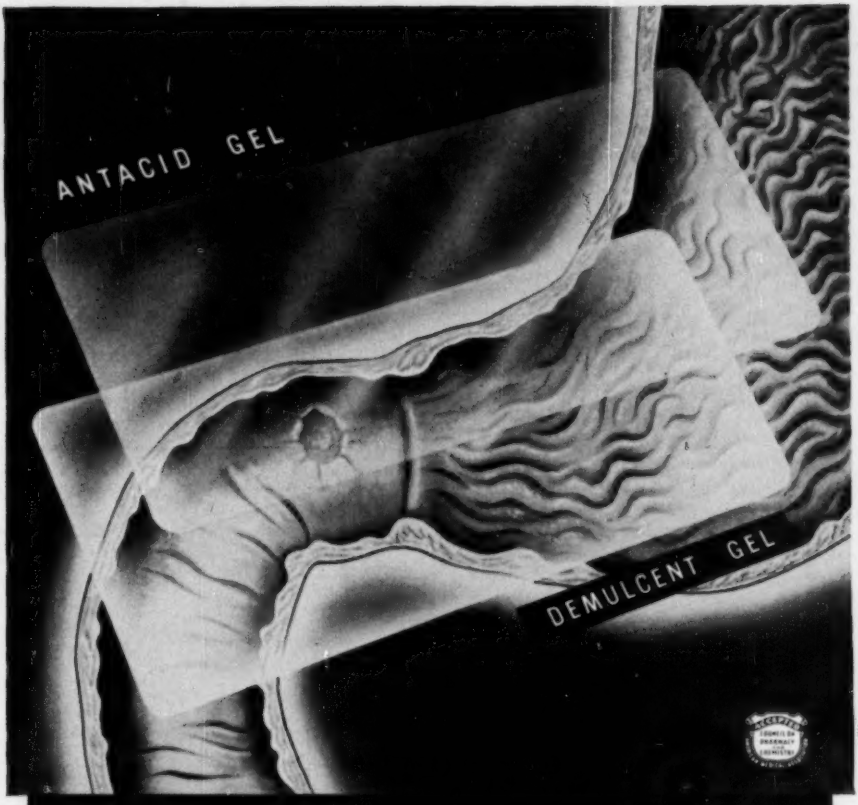

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